ATLAS OF HISTOPATHOLOGY OF THE SKIN

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BY

G. H. PERCIVAL
M.D. Ph.D. F.R.C.P.E. D.P.H.

Grant Professor of Dermatology, University of Edinburgh; Physician to the Skin Department, Royal Infirmary, Edinburgh; Consultant Dermatologist to Edinburgh Municipal Hospitals

A. MURRAY DRENNAN
M.D. F.R.C.P.E. F.R.S.E.

Professor of Pathology, University of Edinburgh; Honorary Pathologist to the Royal Infirmary, Edinburgh; Director of Pathological Services to the Municipal Hospitals, Edinburgh; Director of Scottish Mental Hospital Pathological Scheme

T. C. DODDS
F.I.M.L.T. F.I.B.P. F.R.P.S.

Laboratory Supervisor, Department of Pathology, University of Edinburgh; Lecturer to the Society of Radiographers (Fellowship Course) Scottish Branch

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THIS WORK IS DEDICATED TO

SIR ROBERT McVITTIE GRANT

BART LL.D

TO WHOSE GENEROSITY IS DUE THE FOUNDATION OF THE FIRST CHAIR OF DERMATOLOGY IN GREAT BRITAIN

PREFACE

THIS work is presented in an attempt to portray in pictorial form the microscopical changes found in the more common diseases of the skin. For this reason the text matter has been severely limited just to what seemed necessary to explain briefly the processes illustrated. No references are given: for these and for full discussions of the diseases mentioned, text-books of dermatology or original papers must be consulted. This is, therefore, a companion volume to such works and an introduction to the detailed study of the actual tissues in the laboratory. It is the result of co-operation between the dermatologist, the pathologist and the expert in laboratory technique and colour photography. The dermatologist sees the clinical lesion, its form and distribution; the pathologist sees the finer structure of the actual lesion and compares it with pathological processes as seen in other parts of the body or produced experimentally. Without each worker being in close touch with the other, and each seeing the lesions from both points of view, no undertaking is possible and little advance can be made in a true appreciation of cutaneous pathology.

The Atlas is intended primarily for post-graduate students, and especially those interested in the special study of Dermatology. It should serve as an introduction to the pathology of skin disease, and it is hoped it may stimulate some to pursue the subject by examining their own material. For the general pathologist, who often only sees occasional sections of skin lesions, and these mostly tumours, it may serve as a useful reference.

The majority of the illustrations have been made from the authors' own specimens, but valuable material has also been placed at their disposal, and they wish to thank the following:—Colonel W. G. Harvey, I.M.S., Professor J. R. Learmonth, Professor Stuart McDonald, Junr.,

PREFACE

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Most of the material has been prepared and stained by Mr James Masson with the assistance of Mr James Paul of the Pathology Department of Edinburgh University and Mr Stanley Hay of the Laboratory of the Royal College of Physicians, Edinburgh, to whom our thanks are due for their skill and care.

The colour illustrations were made by the Finlay process, and accurately represent typical areas of the stained sections.

To the block makers we are particularly indebted for the infinite trouble they have taken over the many details and the obtaining of correct colour effects. Also we thank the printers, Messrs McLagan & Cumming Ltd. for the uniform excellence of their work.

Without the constant help and close collaboration of Mr Macmillan and Mr Parker of Messrs E. & S Livingstone Ltd., our publishers, this Atlas could not have been produced.

THE AUTHORS

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INTRODUCTION

In arranging the various skin diseases, the histopathology of which is illustrated and described in the following pages, a clinical classification has been adopted, and they have been grouped according to the type of primary cutaneous change by which they are characterised and not according to their etiology known or presumed. This method has been employed for practical reasons, for skin diseases are much more individually distinct in their clinical aspect than in their pathology and the etiology is in so many cases obscure.

It is of great benefit to portray similar lesions in close proximity for purposes of comparison, because it is graduation of structural alteration which differentiates lesions which otherwise present many features in common both from the clinical and pathological standpoint. To arrange the diseases according to their etiology or the similarity of the course which they pursue, would be to lose this advantage of easy comparison, for a single etiological agent may evoke a variety of pathological changes according to the stage of the disease and the method in which it attacks the tissue. On the other hand, not to do so hampers the opportunity to trace the sequence of variations in tissue response in their continuity throughout the course of the disease. By cross reference however the obstacles presented by either method can be overcome, and it is hoped that while each one may be defective or open to criticism, the classification which has been chosen will prove the least inconvenient.

The histopathology of diseases of the skin can be studied with greater facility than that of any other organ and not only is it possible to correlate the clinical appearance of the eruption with the minute structural changes responsible for it, but the development progress, and regression of these changes can be examined as they proceed throughout the course of the disease. Although histopathology verifies the structural alterations which are suggested by the clinical appearance of the disease, it often happens that the clinical picture is much more striking and distinctive than that revealed by microscopic examination and it is not uncommon for eruptions which present widely different clinical appearances to show almost identical histopathological changes. In these circumstances it is the configuration of the lesions, their grouping, the surface area which they involve, their distribution on the body surface, their persistence, or constant repetition—all of which depend on the causative agent and on the biological state of the individual tissue cells, which give to the eruption its clinical identity and the histological changes offer no explanation for these features. It is therefore a matter for comment and reflection that a limited variety of pathological reactions and their resultant visible microscopic derangements in cutaneous structure can produce a much larger variety of visible clinical manifestations.

The distribution of eruptions which are of known or presumed internal origin presents a problem in itself and no explanation can be offered as to why certain areas of a single tissue should be selected to react with the noxious agent.

The microscopic differentiation of eruptions which are distinctive from the clinical standpoint may rest on minute and delicate findings, and in some cases may be impossible. On the other hand in a limited number of inflammatory diseases, and in the tumours, a precise diagnosis may only be possible when the histopathology of the lesion has been ascertained.

TERMINOLOGY

There are several terms used to indicate certain common abnormalities in epidermal structure and function which are peculiar to cutaneous pathology, and which therefore require to be defined.

ACANTHOSIS. This refers to a general hypertrophy of the rete malpighii, which is accompanied by active mitosis in the cells of its deeper layers. There may be an associated cellular or intercellular oedema. The process usually involves the interpapillary cones of the rete which may be broadened and lengthened with a corresponding alteration in the papillae. As a result of this double alteration in the relations of the papillae and the rete cones it is not uncommon to find on section portions of the papillae cut on such a plane as to appear completely surrounded by epidermis, thus forming the meshes of an apparent network arrangement furnished by the epidermis. The stratum granulosum, lucidum, and corneum need not necessarily be hypertrophied in conjunction with the rete malpighii.

HYPERKERATOSIS This term indicates hypertrophy of the stratum corneum. The cells are normally keratinised and may form a solid mass or they may be loosely arranged to give a basketwork appearance. There is usually an accompanying increase in the layers of the stratum granulosum, but the underlying rete may be normal, acanthotic, or atrophic.

PARAKERATOSIS. In this state the process of keratinisation is upset and the cells fail to undergo the normal morphological and chemical changes as they pass from the rete to the stratum corneum. The stratum granulosum stage fails to develop and the cells reach the level of the stratum corneum in a somewhat swollen condition, imperfectly keratinised, and with their nuclei still present. In this condition they adhere to one another in clumps, which appear clinically as scales. This abnormal process is most commonly intermittent, so that the nucleated parakeratotic clumps of cells appear in layers betwixt cells which have undergone normal keratinisation. Oedema of the rete malpighii or its invasion by leucocytes are the usual visible antecedents and causes of the condition.

Special names have been applied to the varied appearances and effects of intercellular and intra-cellular oedema of the rete malpighi Thus *Spongiosis* is the name given to marked intercellular oedema. *Balloonisation* refers to intra-cellular oedema which causes gross swelling of the cell, and which may be accompanied by amitotic division of the nucleus. Fusion of adjacent cells takes place and results in the formation of large multinucleated cells which are referred to as balloon cells. Vacuolation with subsequent degeneration and disintegration of rete

cells is sometimes referred to as *altération cavitaire*. *Dyskeratosis* is applied to the premature and abnormal keratinisation of individual cells or small groups of cells in the rete malpighii. These cells lose their prickles, become separated from their neighbours, the cytoplasm becomes strongly eosinophilic, and the nucleus pyknotic. On reaching the stratum corneum such cells usually retain their individuality; the pyknotic nucleus persists or becomes fragmented, and they can be identified amongst the surrounding normally keratinised cells. The process affects the entire cell, and is quite distinct from the development of eosinophilic droplets in the cell cytoplasm which is not uncommonly found in isolated cells in a variety of inflammatory and acanthotic processes.

THE SKIN

NORMAL HISTOLOGY

This subject is dealt with in detail in various textbooks of histology and it is, therefore, unnecessary to describe minutely all the features of the normal skin. Here they are demonstrated by a series of illustrations, the descriptions of which will give sufficient detail for an understanding of and comparison with the pathological conditions which follow

Normally the skin forms a waterproof and protective covering for the subjacent tissues and at the various orifices, nose, mouth, etc., it is continuous with the mucous membranes.

The skin consists of the epithelial layer or epidermis, well defined at its deep margin, and the dermis, or connective tissue layer The dermo-epidermic junction is well defined, but the dermis is much less clearly demarcated on its deep surface, which merges with the subcutaneous tissue. The thickness and texture of both epidermis and dermis vary in different parts of the body according to local requirements, e.g. the skin of the sole of the foot is much thicker and denser than that of the body and there are also changes due to age, quite apart from disease.

Related to the skin are its various appendages—hairs, nails, sweat and sebaceous glands, whilst in the dermis are nerves and special nerve endings, blood and lymph vessels.



Fig. 1

Skin from the sole of the foot.—The epidermis is thick and has an especially deep stratum corneum, consisting of many layers of completely cornified epithelial cells from which all nuclei have disappeared and which consist largely of keratin. The layers on the surface are looser and more flaky (*stratum disjunctum*). At the deep limit of the stratum corneum is a thin, pale line, the *stratum lucidum*, consisting of flattened cells filled with eleidin and also devoid of nuclei. Immediately beneath this line is the granular layer or *stratum granulosum*, two to four cells deep. These cells are nucleated, somewhat flattened and contain deeply stained blue granules of kerato-hyalin. Continuous with the stratum granulosum on its deep aspect is the rete malpighii, consisting of several layers of polygonal cells. These cells have well defined nuclei and between them are the intercellular spaces. The intercellular bridges ("prickles") which cross these spaces from cell to cell are not clearly seen except with higher magnification. The cells of the stratum germinativum, the deepest layer of the rete malpighii (rete mucosum), have a columnar form and are known as *basal cells*. The lower limit of the epidermis is well shown and the downward projections ("*rete pegs*") of the malpighian layer are seen to alternate with the papillae of the dermis between them. The dermis consists of collagen fibres amongst which are seen several small capillary vessels. In the centre of the section there is a duct of a sweat gland. In the epidermis the duct appears as several oblique spaces in the cornified layer; in the rete beneath it appears again as spaces between the epithelial cells. There is no special lining to it in these areas and its tortuous character is shown by its being cut in several planes and not as a straight tube. The gland from which this duct springs is not shown.

Hæmalum and Eosin × 75.



FIG. 2

Palm of hand.—This thick section of skin mainly to illustrate the tortuous nature of the sweat glands and their ducts. The coil gland lies deep in the dermis and its duct proceeds to the surface in somewhat corkscrew fashion. A good example is seen to the left of the centre.

Frozen section. Haemalum and Eosin × 15



FIG. 3

Palm of hand.—The epidermis has the usual layers and papillary form of its lower margin. Several sweat ducts are cut in different planes as they run to the surface from the sweat glands—more deeply placed in the dermis. There are also three sensory nerve endings—corpuscles of Vater-Pacini—recognisable by their pale staining and concentric lamination.

Haemalum and Eosin 18



Fig. 4

Sweat glands.—This is higher power view showing the ducts of the glands darker stained and of smaller calibre than the secreting coils. The latter have only small lumen which is lined by cubical to columnar cells one layer deep. A thin basement membrane lies along the base of the cells and there is but scanty supporting stroma around the coils. Just appearing in the field at the bottom is the outer margin of sensory nerve ending.

Haematoxylin and Eosin × 95

APOCRINE SWEAT GLANDS are modified types of sweat glands and are found in the axillae, nipples, public region and around the anus. In the female they have cycles of active secretion followed by resting periods corresponding to the menstrual cycle.



FIG. 5

Section of axillary skin—This shows hair coming to the surface and near its emergence is the duct of an apocrine sweat gland opening obliquely into the hair sheath. The apocrine gland itself is in the lower central part of the field.

Heidenhain Azan Stain 35



Fig. 6

Apocrine sweat gland in its resting stage.—The elements of the gland are larger and have wider lumen than those of the ordinary sweat gland.

Hæmalum and Eosin × 100

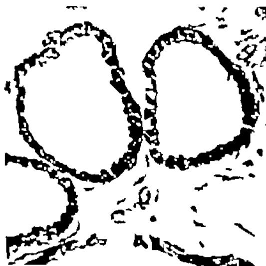


Fig. 7

High power of the same gland to show the type of epithelium.—Closely applied to the base of the epithelial cells there are in places the elongated nuclei of the "myo-epithelial" cells—hich by their contraction are concerned with the expulsion of the secretion.

Hæmalum and Eosin 225



Fig. 8

An apocrine sweat gland in its active phase.—Compare with Fig. 6.
Hæmalum and Eosin × 100



Fig. 9

A.—The same under a higher magnification to show the process of secretion.—The inner zone of the cells becomes granular and disintegrates into the lumen to form the secretion. *B.—Another area of same showing the lumen filled with masses of granules and some cells.* At the margin is a layer which represents all that is left of the partly disintegrated epithelial cells; from these nucleated basal portions a new layer of cubical to columnar cells will develop (see resting stage Fig. 7). *Eosin and Methylene Blue* × 400



FIG. 10

Vertical section of normal scalp.—A low power view mainly to show the disposition of the hair follicles. On the surface is the blue-stained epidermis resting on [illegible] relatively thick dermis continued in the deepest part as fatty tissue. Numerous hair follicles, most of them cut obliquely, are seen running up to the skin surface. At the base of each [illegible] the bulbous growing end of the hair into [illegible]hich projects [illegible] pear-shaped core of dermis which is continuous [illegible]ith [illegible] thin sheath of dermis around the epithelial sheath of the hair shaft.

Celloidin section, Haemalum and Eosin × 25.

SEBACEOUS GLAND This opens into the hair follicle (from which it has arisen) about its upper third and is composed of cells of the rete which become loaded with fatty globules instead of becoming cornified. These fat laden cells disintegrate entirely (= holocrine type of gland) and so form the greasy sebaceous secretion. The glands open into the hair sheaths or on the skin surface by means of a duct lined by squamous epithelium.

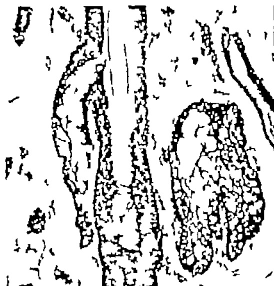


FIG. 11

Opening of Sebaceous gland into hair follicle A hair follicle, with portion of hair within it, has sebaceous-gland duct entering it at one side. On the opposite side is sebaceous gland having the usual characters but no duct is present in this plane

Hewitson and Evans × 100



Fig. 12

Portion of sebaceous gland.—At the periphery of the gland there is thin narrow zone of flattened epithelial cells but as the centre is approached the greater number are transformed into large cells with central nuclei and vacuolated cytoplasm—vacuolated because the fat has been extracted from this section

Haemalum and Eosin × 300



Fig. 13

Frozen section of sebaceous gland, stained for fat.—The lobules consist of solid masses of fat laden cells, the fat being stained yellow (is in the form of neutral fat and no doubly refractile lipoid was demonstrable in this section

Sudan III and Haematoxylin 100

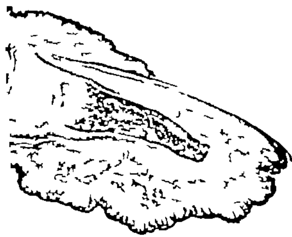


FIG 14

Longitudinal section through nail on toe of infant.—The clear area of the keratinised nail plate is seen on the upper surface of the toe. Its free edge overlaps the epidermis—or hyponychium. Its proximal end is overlaid by the infolded edge of epidermis—or eponychium. The base of the nail lying in the nail groove, reaches nearly to the phalanx and it is covered by its matrix, thin layer of epithelial cells continuous with the invaginated rete malpighi. *Hamilton and Ewen* × 8½

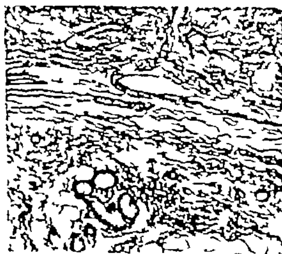


FIG. 15

Transverse section through lateral edge of nail.—This is higher power than the preceding and shows the matrix of malpighian layer with hich the nail plate continuous. Overlapping the edge epidermis with considerable cornification. Underneath the nail plate is thin even line of epithelial cells of malpighian layer. Beneath this the dermis in hich are vessels and nerves seen on cross section. A small portion of phalanx seen below. *Hamilton and Ewen* × 50

Elastic Tissue of Dermis. In addition to the collagen fibres of the dermis there are many elastic fibres distributed between the collagen and around hairs, sweat and sebaceous glands. The amount of elastic tissue varies in different regions and with age.





Figs. 16 & 17

These sections are taken from the palm of the hand and show the whole thickness of the skin from the surface to the subcutaneous fatty layer. In Fig. 16 there is the thick stratum corneum usual for this area, also a thick and dense layer of collagenous fibres amongst which are seen delicate elastic strands, stained black.

In Fig. 17 the deepest layer of the dermis is seen, with smaller elastic fibrils merging with the subcutaneous fatty tissue in which is a sweat gland. Elastic fibrils can be seen surrounding the latter and also ramifying in the loose connective tissue.

Verhoeff and Van Gieson ×75.



Fig. 18

Skin from Abdomen.—The elastic tissue is relatively more abundant than that shown in Fig. 16. A hair and its sebaceous gland have a delicate network of elastic fibres around them.

Weigert Elastin Stain and Van Gieson. × 75.

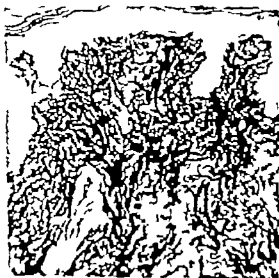


Fig. 19

Skin from Abdomen.—This is a higher power view to show the numerous elastic fibres, their variation in thickness and their close relationship to the base of the epidermis.

Weigert Elastin Stain and Van Gieson. × 400.

NERVES. The skin is richly supplied with nerve fibres, medullated and non-medullated, and by certain special sensory nerve endings. Some of these fibres end on the epithelial cells of the epidermis, some round the hairs, sebaceous, and sweat glands, and still others form vasomotor fibres for the blood vessels. The special sensory organs are numerous about the fingers, hands and toes.



FIG. 20

Skin of volar aspect of finger. Meissner corpuscle.—Situated in papilla of the dermis; an oval body composed of specialised cells around which are wrapped several nerve fibres, which are continuous with those leading away from the corpuscle. *Weddell. Silver Method and Carmine.* × 260



FIG. 21

Skin of tip of finger. Vater-Pacini corpuscle ("Pacinian corpuscle")—Several of these are seen, varying in size and shape, but all consisting of many concentric layers of laminated fibres in the centre of which is the ending of the nerve fibre (not specifically stained in this preparation)

Hæmalum and Eosin × 45.

Both the epidermis and the dermis may be the seat of hypertrophy atrophy and degeneration, atrophy being in some cases the sequel to either of the other two phenomena. The conditions to be considered under this heading are ichthyosis and its variants, cutis laxa, elastosis senilis, and pseudoxanthoma elasticum, all of which may be regarded as physiological deviations—and amyloid infiltration, scleroderma, calcinosis cutis, dermatomyositis, granuloma annulare, and necrobiosis lipoidica—which are, on the other hand, essentially infiltrative or degenerative processes.

In ICHTHYOSIS (Figs 22 24) the epidermis is congenitally atrophic, and its development is altered in such a way as to produce a hypertrophic stratum corneum which on its surface is subdivided by fissures into plates and facets. The associated under-development of the rete extends to the epidermal appendages, which are small and few in number

In CUTIS LAXA (Fig. 25) the elastic tissue shows a regular hyperplasia throughout the dermis. SENILE ELASTOSIS (Fig. 26) and PSEUDOXANTHOMA ELASTICUM (Fig 27) are also characterised by an increase in the amount of the elastic fibres, but in both conditions the fibres are irregularly thickened, whorled, and fragmented, and the process is not uniform but localised to portions of the dermis There is little histological difference between a marked case of pseudoxanthoma elasticum and senile elastosis. Clinically however the former disease is usually distributed on the chest and flexures and occurs in young subjects, whereas senile elastosis affects exposed areas and is seen after the age of forty

AMYLOID (Fig. 28) may occur in the skin as small localised deposits, or it may be diffusely distributed over large areas. In the first instance the deposit exists primarily and solely in the skin, produces an itchy lichenoid eruption, does not result from chronic sepsis in any of the internal organs, and is not accompanied by any deterioration in the general health. In the second instance it is part of a general amyloidosis dependent on chronic suppurative disease elsewhere in the body

In the skin the amyloid occurs superficially in the dermis, first around the capillaries, and later as masses replacing the connective tissue fibres There may be some leucocytic infiltration in the dermis, and the epidermis overlying localised deposits may be hyperkeratotic.

SCLERODERMA (Figs. 29 and 30).—In the early stages, the collagen fibres of the dermis are hypertrophied to form coarse homogeneous bands, there is considerable perivascular lymphocytic infiltration, and the deeper vessels show a diminution in the lumen due to proliferation of the intima and constriction by the swollen collagen. As the disease

progresses these hyperplastic changes gradually give place to atrophy with shrinkage of the skin, fibrosis of the dermis, loss of the papillae, and a thin epidermis

CALCINOSIS CUTIS—The term calcinosis is restricted to the deposition of calcium in the skin with the formation of nodules and the condition is of rare occurrence. It may take the form of discrete nodules situated in the dermis—CALCINOSIS CIRCUMSCRIPTA (Figs 31 and 32) or of an extensive general infiltration—CALCINOSIS UNIVERSALIS

The circumscribed form may be associated with absorptive bone lesions, and, in these circumstances, has been described as metastatic calcinosis In the absence of any preceding or associated impairment of bone formation the condition is regarded as being due to a disturbance of calcium metabolism.

The vicinity of the joints and tendons is the common site for the deposit and it is also sometimes seen in association with scleroderma. The condition has to be distinguished from the calcification which often occurs in sebaceous cysts and in areas of chronic inflammation.

DERMATOMYOSITIS (Figs 33 and 34) presents a picture which suggests a moderate scleroderma as far as the dermis is concerned, but there is an almost complete absence of any infiltration of lymphocytes. The muscles are also affected by the degenerative process and show hyaline change and fragmentation of the individual fibres, with loss of their nuclei.

The clinical appearance of NECROBIOSIS LIPOIDICA (Figs. 38-42) and GRANULOMA ANNULARE (Figs. 35 37) may present a striking similarity and the structural alterations which are revealed by microscopic examination are almost identical. A large proportion of cases of necrobiosis lipoidica occur in diabetics, but the final distinguishing feature between the two diseases is the presence in the dermis of fatty degeneration or infiltration in necrobiosis lipoidica, and the absence of any such change in granuloma annulare. In both conditions there is degeneration and necrosis of the collagen and elastic fibres in circumscribed areas of the middle and lower dermis. The fibres are glassy in appearance and may show basiphil staining, they are fragmented, and nuclear debris is scattered throughout the degenerating patch. Surrounding this area there is a fairly compact infiltration of lymphocytes and histiocytes, which have a palisade arrangement in granuloma annulare. It may be that in the early stages an infiltration of this type precedes the development of the collagen necrosis. In necrobiosis giant cells are not infrequently seen, and deposits of fat are present at the periphery of the necrotic area and to a less extent amongst the fragmented collagen fibres In granuloma annulare localised areas of cellular infiltration similar to those seen in sarcoid have been noted in the vicinity of the necrotic focus



Fig. 22

Ichthyosis.—The supra-papillary portions of the epidermis are narrowed, and the rete pegs are narrow and elongated. The cells of the rete appear compressed and smaller than normal, and the nuclei stain darkly. The stratum granulosum is absent and the ribboned stratum corneum rests directly on the rete. The collagen fibres in the papillary layer of the dermis appear to be homogeneous and stain faintly, and in the deeper portions they are fragmented. Sebaceous glands are much reduced in number and are absent in this section. *Sweat glands are also scanty and the cells of the ducts are flattened.*

Haematoxylin and Eosin × 75



Fig. 23

Ichthyosis Sauroderma type.—The stratum corneum is much hypertrophied. The rete is narrow, the stratum granulosum is absent, and the rete pegs are rudimentary. There is scanty perivascular lymphocytic infiltration. The glandular appendages are few in number.

Hematoxylin and Eosin × 90



Fig. 24

Ichthyosis Sauroderma type.—The collagen and elastic fibres are fragmentary in places, stain poorly, and in general are aggregated into series of horizontal strands.

Verhoeff and Van Gieson × 100



Fig. 25

Cutis laxa.—In this curious condition the skin is abnormally mobile and can be stretched for many inches from its normal position, but it slips back when released. A vertical section shows a great but regular increase of wavy elastic fibres throughout the dermis and extending into the subcutaneous tissue.

Weigert. Elastin Stain and Tartrazine. × 40



Fig. 26

Senile elastosis.—The epidermis is thin. In the dermis, which is reduced in depth, there is relatively large amount of elastic tissue, irregularly distributed in clumps and layers and the collagen is greatly reduced in amount.

Weigert. Elastin Stain and Van Gieson. × 75

PSEUDOXANTHOMA ELASTICUM AND AMYLOID INFILTRATION



Fig. 27

Pseudo Xanthoma Elasticum.—The epidermis is thinned and the rete pegs are absent. In the deepest layers of the dermis there are masses of thickened and fragmented bundles of elastic fibres. Nodules which stain poorly or are vacuolated may be seen here and there in the elastic fibres. No fatty infiltration is to be found in pseudo-xanthoma elasticum. The left-hand portion of the section shows that the increase and coarsening of the elastic fibres not confined to the lower strata of the dermis. The collagen tissue and the skin appendages are normal. There may be slight degree of perivascular lymphocytic infiltration. The condition could be regarded as premature and localised example of senile elastosis with the essential difference that is not associated with fatty degeneration in and amongst the affected elastic fibres. *Verhoeff and Van Gieson* × 65.



Fig. 28

Amyloid infiltration.—There hyperkeratosis, but the essential feature is the violet-stained deposit occupying most of the dermal papillæ, the collagenous fibres being apparently replaced by the amyloid. The vessels are seen running amongst the deposit, but their walls do not show any amyloid. *Methyl Violet* × 55.



Fig. 29

Scleroderma.—The epidermis is thin and the rete pegs are absent. The dermis has homogeneous appearance owing to the fact that the collagen fibres have become thickened and undergone hyaline change.

Haematoxylin and Eosin × 50.



Fig. 29a

Scleroderma.—The same as Fig. 29 to show the thin epidermis and an increase of hyaline collagenous fibres amongst which are fragmented elastic fibres.

Verhoeff and Van Gieson × 75.





FIGS. 30 & 30A

Scleroderma.—The main feature is the very dense dermis, composed of hyaline collagenous fibres amongst which are fragmented, rod-like, elastic fibres—shown up black by the elastic stain in Fig. 32.

FIG. 30—*Haematoxylin and Eosin* × 70.

FIG. 30A—*Verhoeff and Van Gieson* × 70.



Fig. 31

Calcinosis Circumscripta.—Situated in the middle of the dermis there circumscribed deposit of calcium. The collagen fibres immediately surrounding it are abundant and are arranged in regular and concentric fashion; they are in direct contact with the mass. Further away from the deposit the collagen has glassy appearance, probably due to pressure. There are no epidermal elements to be seen in the neighbourhood of the calcium, and there is no sign of inflammation. The epidermis overlying the mass is stretched. *Hamilton and Evans.* 35.



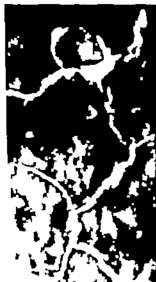


Fig. 32*A* Fig. 32*B*

A.—Medium power view of Fig. 31.—This shows the point of contact between the collagen fibres and the mass of calcium.

B.—High power view of Fig. 31.—Only calcium shown in this illustration. It is in the form of an amorphous mass, throughout which are scattered small crystalline deposits.

Fig. 32 A. *Hamilton and Evans.* 130. Fig. 32 B. *Hamilton and Evans.* × 475.



FIG 33

Dermatomyositis.—The epidermis is thinned and stretched, there is hyperkeratosis, and the rete pegs are absent. The collagen throughout stains poorly. Immediately under the epidermis it is atrophic, while in the deeper areas it is fragmented and there is oedema between the bundles. There no infiltration of inflammatory cells.

Haematoxylin and Eosin 60.



FIG. 34

Dermatomyositis.—The muscle fibres are oedematous and present varying stages of degeneration. The cytoplasm stains poorly and the cells of the sheath have undergone proliferation. There is an infiltration of lymphocytes, and considerable oedema between the muscle fibres.

Haematoxylin and Eosin 300



FIG. 35

Granuloma Annulare.—Low power view showing glassy area of necrotic and fragmented collagen fibres surrounded by well marked cellular infiltration which shows tendency to be arranged in palisade formation.
Hæmalum and Eosin × 50.

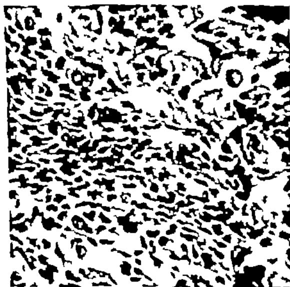


FIG. 36

Granuloma Annulare.—This shows the infiltration surrounding the area of collagenous degeneration. The cells are small lymphocytes and histiocytes.
Hæmalum and Eosin 400



Fig. 37

Granuloma Annulare.—The collagen is fragmented and stains poorly, edema is present, and nuclear debris is scattered throughout the entire area.

Hematoxylin and Eosin × 220

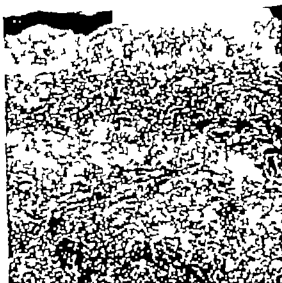


Fig. 38

Necrobiosis Lipoidica.—There is a well defined strip of necrosis of collagen in the middle and lower dermis. The collagen has a glassy appearance, and nuclear debris is scattered throughout its substance. There is peri-vascular cellular infiltration in the vicinity of this area.

Haematoxylin and Eosin × 60.

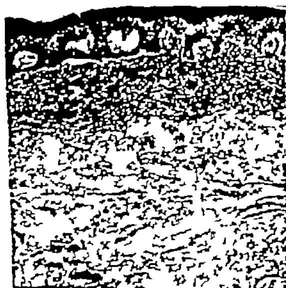


Fig. 39

Necrobiosis Lipoidica.—Similar to Fig. 38, but the necrotic area in the dermis is better defined by the method of staining.

Iron Haematoxylin and Van Gieson × 60



Fig. 40

Necrobiosis Lipoidica.—This is portion of the same lesion shown in Fig. 38. Numerous fat droplets are lying free amongst the degenerated collagen fibres.
Sudan III and Haematoxylin × 55



Fig. 41

Necrobiosis Lipoidica.—This shows an area of necrotic collagen and surrounding infiltration of small round cells. Several "foreign body" giant cells are to be seen in the centre of the section.
Haemalum and Eosin 110.



Fig 42

Necrobiosis Lipoidica—Above, there is an area of fragmented and degenerated collagen containing nuclear debris Below the collagen is swollen, oedema present, and there is an infiltration of lymphocytes and histiocytes

Haematoxylin and Eosin × 350

INFLAMMATION

Inflammation of the skin can be caused by an infinite variety of noxious agents which may reach its tissues either from without or from within, *via* the blood stream In some cases the causative agent is a universal irritant in others its action is only exerted under special conditions of cutaneous predisposition or idiosyncrasy With regard to the former group of irritants, individual skins show a varying susceptibility to their action, some being hyposensitive and some hypersensitive when compared with the average cutaneous sensitivity The intensity of the response depends on three factors, the concentration of the irritant the degree of cutaneous sensitivity of the individual, and the lack of immunity to their action.

In the case of the second group of substances the development of an inflammatory cutaneous reaction depends entirely on the state of the individual skin, the concentration of the irritant being of little importance. In the absence of a suitable state of cutaneous reactivity to which the terms idiosyncrasy and allergy are applied, the tissue is immune to the effects of the agent.

From the standpoint of histopathology inflammation of the skin is only significant when the vaso-dilatation and oedema is accompanied by visible structural or histo-chemical alterations in one or other of the component parts of the skin, or when the cellular reaction which may accompany the vasomotor phenomena presents distinctive characters. It therefore follows that the histological changes found in many of those transient erythematous eruptions, which present a striking and easily distinguishable clinical picture, are merely those of simple inflammation in which special distinctive features as an aid to differential diagnosis are entirely lacking. No individual mention of these eruptions seems necessary in an atlas on histopathology since their microscopic appearance sheds no light on the nature of the process by which they evolve or the causative agents by which they are produced, and the conception of such conditions must meantime be based solely on clinical data. Even in those inflammatory diseases in which distinctive histological changes are found it may be necessary to take clinical facts into account in order to assess the significance of the histological findings and elucidate the method by which they have been produced.

There are three clinical types of Urticaria, namely the common variety designated Urticaria, which is characterised by the transient appearance of wheals Urticaria Papulosa, or Strophulus, which occurs in children and in which the lesions of ordinary urticaria become transformed into papulo-vesicles which erupt in crops and persist for a few days Urticaria Pigmentosa, a rare condition in which the wheals are of a more permanent character than in the two foregoing types, and which is associated with pigmentary changes which persist indefinitely

The clinical lesions of ordinary URTICARIA (Figs. 43 and 44) are striking, but no structural change accompanies them, as they are due entirely to a transient vasomotor reaction involving a dilatation and an increase in permeability of the minute vessels of the papillary bodies, and an arteriolar dilatation. Separation of the collagen fibres by oedematous fluid and perhaps some swelling of the fibres themselves, and stretching of the epidermis is all that is noted histologically There is no cellular reaction.

In URTICARIA PAPULOSA (Figs. 45 and 46) the epidermis shows localised areas of intercellular and intra-cellular oedema, with vacuolation of individual cells in the rete, some of which stain poorly and show pyknosis. The stratum corneum may be thickened and acanthosis with broadening of the rete pegs may be present. There is a decided perivascular infiltration of lymphocytes surrounding the vessels in the superficial vascular plexus.

Urticaria results from the action on the skin of some substance to which the tissue is allergic, the localisation of the allergic process, and hence the clinical type of the reaction, being different from that in eczema. The noxious substance may reach the allergic cells either through the blood stream or as a result of intra-cutaneous inoculation from the outside, such as may occur from the action of stinging plants or biting insects

Urticaria Papulosa is presumed to be an allergic reaction dependent on some unknown toxic agent of internal origin. It should be noted, however that the bites of FLEAS (Figs 49–51) and BUGS (Fig 52) may cause lesions which are identical with those of urticaria papulosa as regards their individual clinical features, but which are differentiated from it by considerations of distribution and course.

In URTICARIA PIGMENTOSA (Figs 47 and 48) there is an increase of melanin in the cells of the basal layer and a varying degree of perivascular lymphocytic infiltration. In addition to lymphocytes, histiocytes and plasma cells are scattered throughout the upper dermis, and a varying number of basophil or mast cells are present, the latter constituting the main diagnostic feature of the lesion. In children, a dense infiltration of mast cells is a characteristic and prominent microscopic feature.



Fig. 43

Urticaria.—The epidermis is stretched but is otherwise normal. There is no vaso-dilatation to be seen, the vessels having collapsed as a result of the rise in the surrounding tissue pressure consequent on the oedema. The collagen fibres are separated by the capillary filtrate.

Haematoxylin and Eosin × 70.



Fig. 44

Urticaria.—The collagen bundles are separated by oedema and present a fine reticular structure. The fibrils themselves are swollen and stain poorly.

Haematoxylin and Eosin 430.



Fig 45

Urticaria Papulosa.—The stratum corneum is thickened and the rete is the seat of inter-cellular and intra-cellular oedema. There is moderate acanthosis, with broadening of the rete pegs. A well marked mantle of lymphocytes surrounds the vessels in the superficial dermis. The collagen bundles are somewhat swollen and separated by oedema. *Hæmalum and Eosin* 80.



Fig 46

Urticaria Papulosa.—The stratum corneum is thickened. The rete is acanthotic and oedematous, the oedema being both intra-cellular, causing vacuolation, and intercellular. The oedematous rete cells stain poorly and the nuclei are pyknotic. There is lymphocytic invasion of the epidermis, and well marked peri-vascular lymphocytic infiltration surrounding the vessels in the dermis. *Hæmalum and Eosin* 160.



Fig. 47

Urticaria Pigmentosa. Adult type.—There is an increase in the melanin content of the basal layer. In the dermis the blood vessels and lymph spaces are dilated, and lymphocytes, plasma cells, histiocytes and basophil or "mast" cells are scattered through it. Giemsa stain × 100.

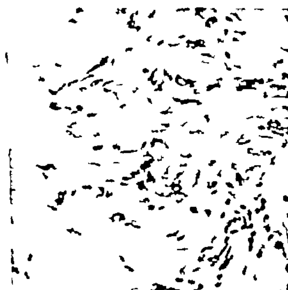


Fig. 48

Urticaria Pigmentosa.—The vessels are dilated and lymphocytes and a few "mast" cells are scattered throughout a slightly oedematous dermis. The section is from a lesion in an adult; in children "mast" cells are much more in evidence. Giemsa stain × 300.

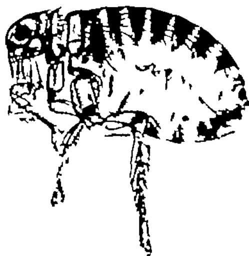


Fig. 49
The Common Flea—Pulex irritans. Adult female.
Cleared Preparation × 18.



Fig. 50
The Common Flea—Pulex irritans. Adult male.
Cleared Preparation × 18.



Fig. 51
The Rat Flea—Xenopsylla cheopis. Adult female.
Cleared Preparation × 25

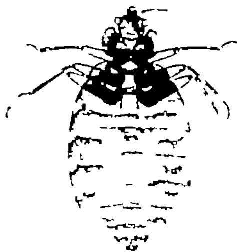


Fig. 52
Bed Bug—Cimex lectularius. An adult male as seen from the dorsal aspect.—The parasite has a mahogany colour as shown.
Cleared Preparation × 8

LUPUS ERYTHEMATOSUS

(Fig. 53)

This condition is characterised histologically by a chronic inflammatory reaction in the dermis associated with degeneration of the collagen and elastic fibres, and secondary atrophic changes in the epidermis.

The vessels of the papillary layer of the dermis are dilated, and there is a sparse perivascular lymphocytic infiltration. In the middle and lower portions of the dermis this infiltration is more dense and forms clumps of cells surrounding the vessels, the sweat glands, and, to a less extent, the sebaceous glands. The elastic and collagenous fibres in the infiltrated area and its immediate surroundings are fragmented and degenerated.

The epidermal changes appear to be secondary to this low grade inflammatory reaction. They consist of thinning and stretching of the epidermis with loss of the rete pegs, and the appearance of hyperkeratosis which forms horny plugs in the mouths of the hair follicles.

The disease is generally regarded as having a definite connection with tuberculosis, and has affinities with the sarcoids and granuloma annulare. Tubercle bacilli and a tuberculous type of cellular reaction are however absent in lupus erythematosus.



FIG 33

Lupus Erythematosus.—The epidermis is stretched and atrophied, and the rete pegs have more or less disappeared. There is hyperkeratosis and the follicles are plugged by masses of keratin. The papillary vessels are dilated, and there is a perivascular lymphocytic infiltration which is scanty in the superficial dermis but dense in the lower and middle portions. The collagen and elastic fibres are destroyed in these lymphocytic clumps.

Hamaker and Eaton × 60

PSORIASIS

(Figs 54 57)

The most striking feature in psoriasis is the development of an extreme degree of parakeratosis, the flattened and nucleated surface cells adhering together to form a succession of layers which replace the stratum corneum. Leucocytes are to be seen scattered throughout the parakeratotic cells both singly and in clumps, the latter resembling minute abscesses. The subjacent stratum granulosum has ceased to exist in many places. The rete is much hypertrophied and there is a pronounced elongation of the inter-papillary processes. The supra-papillary areas are thin, however and the tips of the papillae are separated from the parakeratotic surface only by a few flattened cells (Fig. 55) Here and there polymorphonuclear leucocytes can be seen in the inter cellular spaces of the rete as they wander upwards towards the surface. Some of the rete cells are hydropic, but throughout the epidermis as a whole there is little or no oedema. The papillae may be slightly oedematous, and the vessels are dilated and surrounded by a scanty lymphocytic infiltration. There is nothing to indicate why the extreme and persistent alteration in the process of keratinisation should take place.



FIG. 54

Psoriasis—General view of psoriasis lesion showing the heaped up layered scale containing collections of polymorphs, absence of the stratum granulosum, acanthosis, perivascular lymphocytic infiltration surrounding the terminal capillary loops and the upper arteriolar plexus

Haematoxylin and Eosin × 55



FIG. 55

Psoriasis.—This shows parakeratosis, absence of the stratum granulosum, acanthosis, elongation of the rete pegs, narrowing of the supra-papillary portions of the rete, vascular dilatation of small vessels in the papillae surrounded by lymphocytic infiltration and some oedema

Haematoxylin and Eosin 75

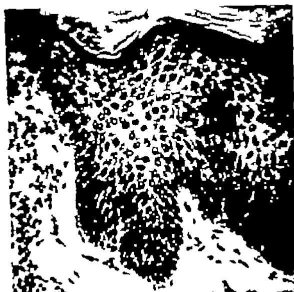


Fig. 56

Psoriasis.—There is irregularity of the stratum granulosum which is absent in places; an acanthotic rete in which the cells are to all appearances normal, few leucocytes wandering through the rete, oedema of papilla, with vascular dilation and perivascular lymphocytic infiltration.

Haematoxylin and Eosin × 200.



Fig. 57

Psoriasis.—The stratum granulosum is absent and replaced by fairly dense collection of polymorphs, the cells of the rete are intact. There is per vascular lymphocytic infiltration in papilla.

Haematoxylin and Eosin 220

PITYRIASIS ROSEA.

(Figs 58 and 59)

While the clinical appearances of the lesions in this disease are distinctive, the associated histological changes are slight and ill-defined. The process is that of a mild inflammatory lymphocytic reaction in the papillary portion of the dermis, with an associated slight inter-and intra-cellular oedema of the rete, which is also invaded here and there by lymphocytes In places the oedema proceeds almost to the formation of small vesicles, and the rete presents a spongy appearance. The stratum corneum becomes ribboned and detached from the underlying rete. The reaction in many respects approaches that of a low-grade eczematous reaction of the flexural infective type, and as such can be classed, both from the clinical and histopathological standpoint, as an eczematide.



Fig 58

Pityriasis Rosea.—The stratum corneum ribboned and detached from the rete, there is some parakeratosis, and the rete is the seat of slight intercellular oedema. There is some vascular dilatation and perivascular lymphocytic infiltration in the papillary portion of the dermis. *Hamilton and Eaton* ×70



Fig 59

Pityriasis Rosea.—This shows an area of intercellular oedema in the rete, associated h intracellular oedema and vacuolation of the cell protoplasm. In some cases rete cell seems to have liquefied completely leaving vacant space, and the area is invaded by lymphocytes. I the papillae the vessels are dilated and there is an infiltration of lymphocytes. *Hamilton and Eaton* ×300

LICHEN RUBER.

The lesion of lichen ruber is a dermo-epidermic papule, which on account of variations in localisation and secondary changes, can be so modified as to produce four distinct varieties of the disease, namely LICHEN RUBER PLANUS (Figs 60-62), the most common type LICHEN RUBER VERRUCOSUS (Fig 63), LICHEN RUBER ACUMINATUS (Fig 64), LICHEN RUBER PEMPHIGOIDES (Figs 65 and 66), an extremely rare modification.

Certain histological features are predominant in all these varieties, and are most clearly seen in *lichen ruber planus* The stratum corneum is thickened in a regular fashion, and parakeratosis is absent except in lesions of old standing The stratum granulosum is increased in thickness, sometimes consisting of five to eight layers of granular cells, but the hyperplasia does not occur uniformly being accentuated in some places and little evident in others. The hypergranulosis is evident clinically in the fine network of white lines which can usually be seen on the surface of the papules. The rete is acanthotic and the pegs are flattened. There is a closely packed infiltration of lymphocytes in the papillary layer of the dermis, and this infiltration is sharply delimited at its deeper and lateral margins. The cells tend to invade the epidermis in the region of the basal layer so that the dermo-epidermic junction is obscured and hazy in places. The tips of the papillae are oedematous, and as a result they become dome shaped, and this, together with the flattening of the rete pegs, causes the dermo-epidermic junction to assume the form of a series of flattened arches. Small collections of fluid may accumulate just underneath the basal layer causing it to split off the dermis, and one of the sections illustrated shows this process accentuated to such a degree as to constitute a bulla, although none was apparent clinically and its presence was not expected in the histological preparation. In the deeper part of the dermis there may be a slight lymphocytic infiltration surrounding the coil glands.

In rare cases the fluid may collect in the rete and raise the thickened stratum corneum so that a clinical and histological intra-epidermic bulla is formed—*lichen ruber pemphigoides*

In *lichen ruber verrucosus* the same epidermal and dermal changes are present as in lichen ruber planus, with, in addition, the upward development of papillary epidermal projections and the formation of horny plugs between them.

In *lichen ruber acuminatus* the lesions have a follicular localisation. Plugging of the mouths of the follicles is conspicuous and the adjacent epidermis is atrophic, probably on account of its being squeezed between

the horny plug above and the infiltration below Lichen ruber acuminatus may show a clinical resemblance to the mild variety of pityriasis rubra pilaris. The histological difference between the two diseases is quite distinct, for the circumscribed subepidermic lymphocytic infiltration which is characteristic of lichen ruber is absent in pityriasis rubra pilaris.



Fig. 60

Lichen Ruber Planus.—There is hyperkeratosis and hyperplasia of the stratum granulosum, which is more prominent in some places than in others; flattening of the rete pegs; dome shaped papillae which are oedematous; dense circumscribed lymphocytic infiltration in the papillary layer of the dermis, invading the basal layer in places, so that the dermo-epidermic junction is ill defined; here and there small collections of fluid are to be seen immediately beneath the basal layer, causing clear spaces.
Hamaden and Eame × 60



Fig. 61

Lichen Ruber Planus.—Hyperkeratosis and thickening of the stratum granulosum are present. The rete pegs have disappeared, and some of the cells in the deeper strata of the rete are vacuolated. The dermo-epidermic junction is hazy. The papillary layer of the dermis is packed with lymphocytes and elastic fibres are absent in this area. In the deeper portions of the dermis the collagen and elastic fibres are normal in structure and staining properties. *Verhoeff and Van Gieson* × 80



FIG. 62

Lichen Ruber Planus.—This section shows large collection of exudate immediately underneath the epidermis. Small collections of fluid are commonly seen in this area. The clinical lesion did not present the appearance of bulla.
Hæmalum and Eosin × 70.



Fig. 65

Lichen Ruber Pemphigoides.—An intra-epidermic bulla has formed, which is roofed by the stratum corneum. Otherwise the usual features of lichen ruber planus are to be seen.

H[illegible] and Evans × 12



Fig. 66

Lichen Ruber Pemphigoides.—The roof of the bulla is formed by the stratum corneum, and some lymphocytes are present in its cavity. The hyperplastic stratum granulosum seen at the periphery of the bulla, and the sub-epidermic lymphocytic infiltration is seen invading the deeper layers of the epidermis.

H[illegible] and Evans 90

PITYRIASIS RUBRA PILARIS

(Figs. 67–69)

This appears to be essentially a disease of the epidermis, characterised by a general hypertrophy of all its layers associated with follicular plugging. The condition may be confined to certain areas of the skin surface, or it may become generalised. In the more extensive cases the epidermal change is associated with vaso-dilatation and perivascular infiltration, mainly lymphocytic in type, and the clinical picture is that of a generalised erythrodermia. When an inflammatory phase is in progress on localised areas the disease bears some resemblance to psoriasis, and when in the purely hyperkeratotic and acanthotic types there is a slight tendency to congestion round the orifices of the hair follicles the small lesions may at first sight suggest lichen planus.

Histologically there is a varying degree of acanthosis, associated with marked hyperkeratosis. The grossly thickened stratum corneum dips down into the rete so that the junction between the two zones is represented by a wavy line, and it also distends the mouths of the follicles with horny plugs which may show a whorled arrangement, and which cause some thinning of the rete. The stratum granulosum is uniformly thickened. There may be little or no vascular or cellular reaction in the dermis, and when present it is limited in the mild forms of the disease, to the region of the hair follicle. The cellular infiltration consists mainly of lymphocytes and maintains a perivascular localisation, showing no tendency to collect into masses such as occur in lichen planus

In the generalised erythrodermatous stage of pityriasis rubra pilaris the epidermal changes are similar to those seen in the milder form, although horny plugs may develop apart from the follicular orifices The vascular dilation and perivascular infiltration are more uniformly distributed throughout the upper dermis. In both types of the disease the sebaceous glands tend to be atrophic, and the sweat glands scanty



Fig 67



Fig 68

Fig. 67.—*Pityriasis Rubra Pilaris.*—There is general acanthosis, the stratum granulosum is enlarged, and the stratum corneum is many times its normal thickness and dips downwards in places into the rete. There is no vascular or cellular reaction to be seen.

Haemalum and Eosin × 60

Fig 68.—*Pityriasis Rubra Pilaris.*—This section is from a case showing large areas of erythroderma. The usual epidermal features are present; the horny cone has developed in relation to a sweat gland orifice. There is diffuse vascular dilation and perivascular infiltration by lymphocytes in the upper dermis.

Haemalum and Eosin × 70.



Fig 69

Pityriasis Rubra Pilaris.—The mouth of a hair-follicle is plugged and the stratum corneum forming the plug has a whorled arrangement. There is vascular dilatation and perivascular infiltration of lymphocytes along the line of the follicle.

Haemalum and Eosin × 80

Eczema is such a complex subject that it has been thought appropriate not merely to indicate the bare structural changes which it presents, but to correlate them with the clinical manifestations of the disease, and to attempt an analysis of the mechanism by which they have been brought about. A certain part of the explanation offered is applicable also to the vesiculo-bullous diseases as a whole.

The "Eczema" reaction is one of the most common examples of cutaneous allergy and the extraneous exciting agent which reacts with the intolerant tissue may reach it from the outside, or from within, *via* the blood stream. Many such agents have been conclusively identified, and many others are suspected with more or less justification, but little is known of the associated biological changes which occur in the tissue cells.

Eczema is an epidermo-dermic reaction which is capable of showing rapid variations in both its clinical appearance and in the histological changes which it presents. To the naked eye the reaction may show three well-defined states, taking the form either of a vesicular eczema, a weeping eczema or a scaly eczema. The scaly phase is common to all eczemas prior to their disappearance, and a weeping eczema may or may not be preceded by one showing clinical vesiculation. From the clinical standpoint these three modifications constitute stages of a single and uniform type of inflammatory response. While the reaction itself is limited in its phases it presents additional individual characteristics according to the exciting agent. This factor determines the site on which the reaction develops or for which it shows a preference, its mode of onset and spread, the contours which it assumes, its duration, and the surface area which it affects, so that it is possible to subdivide the majority of cases of eczema into three well-defined groups. These are as follows —

(1) Chemical eczema (2) infective eczema, which can be further subdivided into flexural infective eczema, post traumatic infective eczema and follicular infective eczema, the two latter groups being characterised by nummular patches on non-flexural areas (3) diffuse papular eczema, including Besnier's Prurigo.

To avoid confusion due to a possible misunderstanding of the clinical classification of the disease which has been adopted, and which is to be correlated with the histopathological illustrations, a brief clinical resumé will perhaps be advisable.

By chemical eczema is meant an eczema reaction evoked by external contact with a chemical substance to which the skin is allergic or intolerant. In these circumstances the reaction assumes its most typically vesicular form, the vesicle roofs are intact, and as a result there

may be little mitial redness, even though the capillaries are markedly dilated. The presence of a flare forming a halo to the main centrally placed vesicular reaction indicates an accompanying arteriolar dilation. The site of chemical eczema depends on the site of contact of the chemical.

Flexural infective eczema occurs in the body folds and creases. It develops slowly and presents a clear-cut well-defined edge, without a surrounding arteriolar flare. Formed vesicles are scarcely to be seen, and then only in the earliest stages. Their place is taken by pinhead-sized pits in the surface, which ooze copiously and intermittently in the acute phase.

Both varieties of nummular infective eczema are most commonly seen on the backs of the hands and forearms and consist of one or more round patches, which have a clear cut margin, and no surrounding arteriolar flare. As crusting is a prominent feature, formed vesicles are not often seen, and vesiculation proceeds underneath the crusts. The vesicle roofs are poorly formed and easily rubbed off revealing superficial pits. The lesions in this type of eczema develop at localised points and enlarge slowly at their periphery

While the preceding varieties are regarded as being due to excitants acting on the skin from the outside, in generalised papulo-vesicular eczema an internal origin is more probable. The eruption shows a symmetry of distribution and a constancy in the sites it involves (e.g.—Infantile eczema, Besnier's prurigo) In type it consists of numerous papulo-vesicular nummular patches or isolated small groups of papulo-vesicles These are well-defined in outline, and a marginal flare is seldom present. The course of the eruption is prolonged and characterised by exacerbation and remission.

The most striking structural alterations associated with eczema are to be seen in the epidermis, where the repeated formation of multiple vesicles, evidence of their attempted formation, or the presence of changes which are related to their formation or previous existence, constitute the basic and predominant histological features of the reaction.

Newly formed vesicles give the appearance of clear spaces in the epidermis which vary in size according to their stage of development, and according to whether coalescence between neighbouring vesicles has taken place The interior of the vesicle is clear except for a few lymphocytes an occasional leucocyte, and degenerated epidermal cells—which are swollen, stain poorly show pyknotic nuclei or are anuclear and which occur singly or in small clumps (Fig 70) These vesicles may occupy almost the entire substance of the rete mucosum, or be situated about its middle or superficial third, and they occur both in the suprapapillary portion and in the interpapillary pegs The cells forming their walls are usually flattened but may be swollen and present a degenerated appearance (Fig. 71). The rete in the neighbourhood and underneath the vesicle may be firm and compact (Fig 73), or it may show intercellular oedema,

with the intercellular spaces much widened and the prickle cells stretched apart (Fig. 77). In some cases the vesicle is separated from the dermis only by a single layer of raggedly arranged and degenerating epidermal cells. In addition to intercellular oedema there may be areas where the cells are hydropic and appear to be saturated with fluid, and in which the nuclei show pyknosis and fragmentation, or have disappeared (Fig. 71) The roof of the vesicle may consist of an intact stratum corneum (Fig 70), or the vesicle contents may have burst into it, separating its layers (Fig. 72) On the other hand the roof may be composed of para keratotic cells, a formed stratum corneum being absent (Figs. 81 and 82). In the latter case the vesicle contents easily reach the surface where they coagulate and desiccate, and form into a large crust which covers a number of vesicles (Fig 75). The crust may show alternating areas of coagulated tissue-fluid and parakeratotic cells, the whole overlying a vesicular rete—a picture which indicates the repeated and successive formation of vesicles and the continuing nature of the reaction (Fig 78)

The epidermis overlying the papillae may be represented merely by a few widely separated, degenerated cells, so that there appears to be a direct communicating channel between the oedematous and congested papilla and the exterior (Figs. 83 and 88).

The whole epidermis may be acanthotic, and when this occurs numerous cells in the area show active mitosis (Fig. 80).

In the papillary portion of the dermis the capillaries are dilated, the papillae may be oedematous, and the degree of oedema may sometimes be extreme (Figs. 81 82 and 84) There is a variable amount of perivascular lymphocytic infiltration. On the whole, however the dermal changes may be extremely slight, even when the clinical intensity of the reaction is considerable and the most striking changes and extreme structural alterations are to be found in the epidermis (Fig. 70).

The rapidity with which these structural changes may develop is illustrated by Fig 70, which shows fully developed vesiculation within twelve hours of contact with the exciting cause, and in Fig. 86 which shows a reconstitution of the cellular disturbance depicted in Fig 85 within a period of thirty-six hours. In urticaria even more rapid changes from normal to pathological and vice versa are to be seen clinically but in urticaria gross structural alterations and evidence of cellular damage are absent (Fig. 43 Urticaria), and the lesion depends entirely on a vasomotor reaction involving transient but gross variations in capillary filtration.

The foregoing is a general review of the disorganisation of the cutaneous structure which constitutes the eczema reaction, but just as there are clinical modifications which allow the disease to be divided into three main groups, each of which seems to depend on the nature of the exciting agent, so it is found that the histological picture is correspondingly modified in each of the groups, some of its features being accentuated, others being partially in abeyance.

These particular modifications in the general character of the eczema reaction can readily be appreciated from the illustrations, which have been arranged according to the type of case from which the tissue was obtained. Thus in chemical eczema vesiculation takes place under an intact stratum corneum and is seen in its most complete and highly developed state.

In nummular infective eczema vesiculation occurs superficially in the epidermis and the vesicle contents escape early on to the surface to dry up and form a crust, under which the process continues Gross surface infection of a secondary nature may be responsible for the development of a dense leucocytic infiltration (Fig 79), but, although eczema of this type is presumed to be in part at least of bacterial origin, a leucocytic reaction is a rare accompaniment.

In flexural infective eczema oedema of the papillary portion of the dermis may be extreme (Fig 84) and cellular oedema of the epidermis is much in evidence (Fig 85). The vesicles are small, situated superficially in the epidermis, and roofed by degenerated cells, or by dried serum (Figs. 81 and 82). Considerable disintegration and atrophy of the whole epidermis may be apparent in long standing cases (Fig 87) The most distinctive feature in this type of eczema is the loss of epidermal cells at the tips of the papillae, with the formation of channels leading from these structures to the surface, which are evidenced clinically as "pits" (Figs 83 and 88).

The fact that both nummular infective eczema and flexural infective eczema present an intense redness from their commencement is due not only to vaso-dilatation, but to the early loss of the capacity to form a stratum corneum.

In the diffuse papulo-vesicular type the structural changes vary between those of a nummular and a flexural eczema.

It may be objected that these three characteristic modifications of a general histological picture merely indicate its consecutive or inter related phases and there is no doubt that each modification may predominate at some stage in the same patch of eczema. Nevertheless the clinical groups with which they are constantly associated present such individuality in their rate of development, course, response to treatment, and as far as can be ascertained as regards their cause, that any structural modification which is in a general way peculiar to any one of them should meantime be regarded as significant and as having some relationship to the biological processes by which the reaction has been brought about. Furthermore they may be interpretated as bearing the imprint of the general character of the causative agent. That they do not depend entirely on the peculiarities and susceptibilities of an individual skin is demonstrated by Figs. 73 80 and 88, which show the three modifications due to different exciting factors, occurring almost simultaneously in the same patient on separate sites. On the other hand a transformation from one type of reaction to another may occur in the same eczema lesion thus a nummular eczema may assume the clinical and histolo-

gical features of a flexural type of reaction. It is difficult for a typical chemical type of reaction to develop on a pre-existing nummular or flexural type, because of the already existing epidermal changes and the absence of a stratum corneum. What happens in these circumstances is an exaggeration of the existing reaction, with a tendency for it to assume the flexural type with pits, and the development of a typical chemical reaction in the immediately surrounding intact skin.

THE FACTORS INVOLVED IN THE PROCESS OF VESICULATION

The mechanism by which the recurrent vesiculation of eczema is brought about can be deduced to some small extent from a study of the histopathology of the reaction in its various forms and stages, from a consideration of the associated clinical data, and from a comparison with these factors as they obtain in other superficial exudative inflammatory diseases. If the size of the vesicle in Fig. 70 is compared with the adjacent rete it is obvious that the area now occupied by the vesicle must have been represented originally by a large number of cells. It is *difficult to conceive that an influx of capillary filtrate from the dermal* capillaries could have overcome existing intra-epidermal tissue pressure and exerted sufficient hydrostatic pressure to disrupt the normal inter cellular cohesion of the rete cells with the formation of a fluid-containing space of such dimensions, in the absence of other factors. There is no constant or gross intercellular oedema in the cellular layer forming the floor of the vesicle to suggest a passage of filtrate actually an examination of the eczema vesicles illustrated, and of Fig. 122, which shows the base of an impetigo bulla, reveals the fact that intercellular oedema may be entirely absent in this area. The cells forming the walls of the vesicles are flattened and closely approximated, and the layer of flattened cells is not extensive. These facts suggest that the cavity is in part the result of liquefaction of rete cells, and to support this hypothesis there is visual evidence of localised groups of rete cells well advanced in degeneration (Fig. 74). That there is localised increase in tissue fluid, and a disturbance in its distribution is shown by the localised areas of intercellular oedema (Fig. 77) and by evidence of oedema in the papillary portion of the dermis (Figs. 81 8., 83 84 85 and 87).

An increase in capillary filtrate is brought about by an increase in the permeability of the capillary wall, in the hydrostatic pressure within the capillaries, and in the rate of blood flow through them, which in turn is dependent on the state of dilatation of the arterioles. In all forms of eczema the capillaries are dilated. In chemical eczema a flare is seen at the periphery of the lesion, indicating an accompanying arteriolar dilation, but in nummular and flexural eczema there is no such flare to be seen at the edge of the lesions so that in these types no arteriolar dilation of any significance can exist, and an increase in capillary pressure and rate of blood flow from this cause cannot take place. A similar absence of flare is seen in the fresh bullae of pemphigus. Capillary

dilatation without a simultaneous arteriolar dilatation or venous occlusion can only result in a fall in capillary pressure so that hydrostatic pressure can play little active part in the localised accumulation of fluid, and from the vascular side an increase in the permeability of the capillary walls can be the sole operative factor in bringing this about.

An increase in hydrostatic pressure, in the rate of blood flow and in capillary permeability all occur in ordinary urticaria, and the result is a localised transient oedema of the papillary portion of the dermis. (Fig 44).*

If in urticaria, where the most favourable conditions exist for the development of increased capillary filtration, the filtrate is limited to the dermis, where it so increases tissue pressure that the hydrostatic intra-capillary pressure is ultimately overcome and the capillaries collapse, and yet the epidermis is not normally penetrated, it is obvious that changes in hydrostatic pressure relations in the eczema reaction cannot alone account for the presence of fluid in the epidermis. In eczema the dermal tissue pressure does not rise sufficiently to overcome capillary pressure. The factor which attracts fluid into the epidermis must therefore be some physico-chemical force which has developed as a result of the localised necrosis and liquefaction of epidermal cells, a state of affairs which is revealed by histopathological study

In eczema the variable degree of epidermal and dermal oedema seen in different specimens in association with equally well developed vesicles, the histological evidence that vesiculation is a continuously repeated process *in situ* and the known rapidity with which structural changes can occur suggest that the flow of tissue fluid into the epidermis occurs intermittently and that the process is somewhat as follows —Multiple localised foci of epidermal necrosis are produced in association with or as a result of the allergic process. A physico-chemical force develops in these areas and sucks the adjacent tissue fluid to them, capillary permeability is increased and the filtrate is also pulled to the necrotic areas. The passage of the capillary filtrate through the epidermis to localised points is evidenced by transient intercellular oedema. The commencing localisation of this fluid, together with that derived from liquified epidermal cells in a commencing vesicle is also responsible for the temporary appearance of intercellular oedema, which is soon replaced by a pool of fluid as the vesicle matures. The increasing hydrostatic pressure within the developing vesicle gradually overcomes the attracting force, and the movement of fluid within the epidermis stops for the time being, the size of the vesicle being limited by the elasticity of its walls and by the surrounding tissue pressure. The entire process is repeated by the development of fresh areas of epidermal necrosis again upsetting the equilibrium of the tissue fluid and capillary filtrate.

* Bullous urticaria [illegible] of such rare occurrence and obviously involves factors which are absent in ordinary urticaria that [illegible] requires special consideration and can be excluded from the present comparison

A comparable periodicity of an allergic process is known to occur in urticaria where there is complete clinical disappearance of the lesions between the attacks In urticaria a rapid reabsorption of the capillary filtrate in the dermis is possible, due to the influence of the colloid pressure of the blood plasma, for there is no histological evidence of damage to cellular structures such as would add colloid to the exuded filtrate and so hinder its reabsorption. The lymph vessels offer a further channel for absorption, and the filtrate surrounds these vessels and the capillaries, or is in their near vicinity In eczema the fluid eventually concentrates at a distance from the vascular and lymphatic systems, is separated from them by compact cellular tissue, its colloid content is considerable, therefore reabsorption does not take place.

In urticaria there is a periodic transient diffuse soaking of the upper dermis with capillary filtrate, associated with the temporary development of increased tissue pressure. In eczema there is probably a similar periodic transient soaking of the epidermis with capillary filtrate, which is at first diffuse but which is rapidly concentrated in localised areas to form, along with the liquified epidermal cells, the vesicles which are typical of the reaction. The type of modification of the reaction which is associated with the individual clinical groups must depend on the nature and site of the initial cell damage which in turn must be governed by the exciting factor and the dominant features of the allergic process. The fact that reabsorption of the oedema in eczema is difficult, with the result that restitution of the damaged tissue to normal is slow may tend to render the vascular phenomena associated with it more continuous than in urticaria.

This conception of a periodicity in the fluid movement in eczema comparable to that which from clinical observation, is known to occur in urticaria, would account for the varying pictures of vesiculation with and without an accompanying intercellular and papillary oedema, the presence or absence of which would depend on the state of activity of the eczema process at the time of removal of the tissue for examination.

The ultimate fate of the unabsorbable fluid collections in the epidermis is either extrusion to the exterior by rupture of the vesicle roof or desiccation *in situ*, the determining factor being the site of the vesicle in the epidermis and the integrity of the tissue forming its roof The state of the cellular layer forming the roof of the vesicle depends in turn on whether the reaction takes place in a hitherto intact epidermis, or in one which has been subject to recurrent oedema. In the latter case the tissue in which the factors necessary for vesicle formation develop may be in such a state of disintegration that only imperfect or abortive vesiculation is possible (Fig. 87), and indeed there may be direct communicating channels conducting the capillary filtrate from the papillae to the exterior It has already been noted that this latter development is peculiar to flexural infective eczema, in which the

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transient nature and periodicity of the increase in capillary filtrate can be observed clinically in the sudden alternation of dry and wet phases

Similar factors may govern not only the final disposition of the eczema vesicle, but also that of the vesicles and bullae of dermatitis herpetiformis, herpes zoster herpes simplex pemphigus, impetigo and varicella.

In eczema as soon as the oedema subsides the epidermal cells rapidly become reconstituted as a compact mass, and as a result of mitosis the entire rete becomes thickened (acanthotic) (Fig 86), but it may be some considerable time before the normal mode of evolution of the cells from the basal layer to the surface is re-established and a normal stratum corneum produced. During this stage of retrogression the surface is composed of a parakeratotic layer and the eczema is clinically in a scaly stage. If the eczema reaction repeatedly attacks the same area, the latter may become hypertrophied (Fig. 91 lichenification), but as this is by no means a constant sequel it would seem that some further cutaneous peculiarity is necessary for its occurrence. It is seen in its highest degree of development in the chronic constitutional eczema known as Besnier's prurigo, a condition which not infrequently occurs in association with ichthyosis, and one which is often accompanied by asthma.



Fig. 70

Chemical Eczema.—Vesiculation is fully developed within twelve hours of contact with the irritant (mercury), and involves almost the entire thickness of the epidermis. The stratum corneum is intact. The cells in the immediate vicinity of the vesicle are flattened. There is no obvious dermal oedema, the vessels are dilated and there is moderate perivascular accumulation of lymphocytes. *Hæmalum and Eosin.* × 100



Fig. 71

Chemical Eczema.—A high power view of the septum between the large vesicle in Fig. 70 and the smaller one situated on its right side. The cells are flattened, the cytoplasm is oedematous and stains poorly, the nuclei are pyknotic, an area of necrosis and liquefaction with loss of cell outline and nuclei is to be seen in the bottom right hand portion. The vesicle cavities contain lymphocytes, degenerated epidermal cells (top left), and cell debris. *Hæmalum and Eosin.* × 275.



Fig. 72

Chemical Eczema.—Eczematous reaction to mercury twenty-four hours after contact showing a well formed vesicle rupturing into the layers of a normal stratum corneum. With the exception of some intercellular edema and necrosis of individual epidermal cells at the base of the vesicle, the surrounding rete is remarkably intact.

[illegible] and [illegible] × 275



Fig. 73

Chemical Eczema.—Showing the same structural changes as in Figs. 71 and 72.

[illegible] and [illegible] × 100

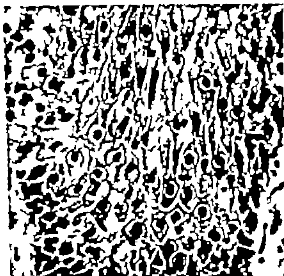


Fig. 74

Chemical Eczema, commencing vesicle.—The prickle cells are edematous, vacuolation much in evidence, the nuclei are pyknotic and in some cells they have disappeared; few mononuclear cells are in process of disintegration.

Hematoxylin and Eosin ×420

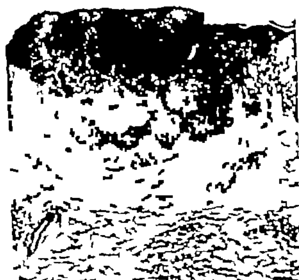


FIG. 75

Nummular Infective Eczema.—A small patch of nummular infective eczema of thirty-six hours duration. A large mass of dried exudate rests on an eczematous epidermis in which are a number of small vesicles and areas of intercellular oedema. The dermis shows dilated vessels and a slight perivascular lymphocytic infiltration.
Haemalum and Eosin × 75.

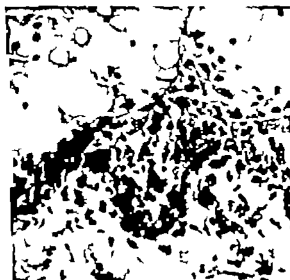


FIG. 76

Nummular Infective Eczema.—High power view of the epidermis underlying the crust in Fig. 75. It shows intercellular oedema, multiple small vesicles containing degenerating epidermal cells, and lymphocytes within the vesicles and penetrating the epidermis.
Haemalum and Eosin × 350.

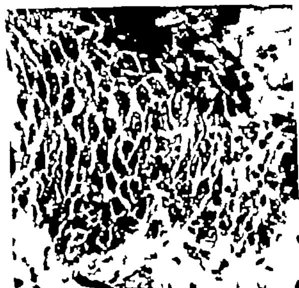


Fig. 77.

Nummular Infective Eczema.—A high power view of the epidermis underlying the crust in Fig. 75. It shows intercellular edema, intracellular edema, degeneration and disappearance of individual epidermal cells, and invasion by a small number of lymphocytes. *Hematoxylin and Eosin.* × 350.



Fig. 78.

Nummular Infective Eczema.—*Nummular patch of eczema of six weeks' duration.* There is a crust of dried exudate on the surface resting on a layer of parakeratotic surface cells. A vesicle is present superficially in the epidermis and contains degenerated epidermal cells and a few lymphocytes. The contents of the vesicle are rupturing into the parakeratotic surface. The epidermis forming the base of the vesicle shows intercellular edema, degeneration of the epidermal cells, and infiltration by lymphocytes. The whole picture indicates recurrent vesicle formation. *Hematoxylin and Eosin.* × 275.



Fig. 79

Nummular Infective Eczema.—*Nummular patch of twelve weeks' duration.* The alteration in structure is similar to that shown in Fig. 75 but there [illegible] great leucocytic reaction in the superficial derma, indicating secondary infection with organisms which have no connection with the production of the eczematous reaction.

Haemalum and Eosin × 100



Fig. 80

Annular Infective Eczema.—Showing the same structure as Fig. 75 and in addition considerable acanthosis.

Haemalum and Eosin × 50



Fig. 81

Flexural Infective Eczema of axilla of one month duration.—This shows multiple small vesicles situated very superficially in the epidermis and roofed by a thin layer of sodden flattened nucleated cells. There are degenerated epidermal cells in several vesicles. Intercellular oedema is visible on one side of the papilla, but there is a compact rete on the other side. A dilated capillary appears in the papilla surrounded by lymphocytes which are also invading the rete. *Haxthausen and Evans.* 225



Fig. 82

Flexural Infective Eczema.—An adjacent field to that shown in Fig. 81 showing similar vesiculation, acanthosis, and areas of rete cells undergoing degeneration and soaked with exudate. There is considerable oedema in the papillary layer of the dermis.
Haxthausen and Evans. 120



FIG. 83.

Flexural Infective Eczema.—An adjacent field to those shown in Figs. 81 and 82. Here there is a channel leading from the surface to the tip of a papilla—an eczema pit. The adjacent rete to the right shows superficial vesiculation, the underlying rete being normal in structure. (*Haxthausen and Eaton.*) × 300.



FIG. 84.

Flexural Infective Eczema.—From the same case of acute weeping eczema of the axilla as in Fig. 81 to Fig. 83. There is no vesiculation to be seen in this field, but the more superficial cells in the rete stain poorly. Gross papillary oedema is the striking feature. (*Haxthausen and Eaton.*) × 90.



Fig. 85

Flexural Infective Eczema.—From a case of acute weeping eczema of the retro-auricular region, of four days duration. There is marked intercellular oedema and cell degeneration, the stratum corneum is replaced by a layer of flattened nucleated cells and the papillæ are oedematous. *Hæmalum and Eosin.* × 275.



Fig. 86

Flexural Infective Eczema.—The same case as Fig. 85, thirty-six hours after treatment with wet dressings of 0.5% solution of silver nitrate in distilled water. Epidermal and papillary oedema have subsided and there are no areas of cell degeneration in the epidermis. The rete forms a compact mass, has become acanthotic, and a stratum corneum is attempting to form. *Hæmalum and Eosin.* × 100.



FIG. 87

Flexural Infective Eczema.—From case, primarily affecting the retro-auricular regions and groins, which became generalised. The duration of the disease was two years, and recovery was satisfactory. The specimen illustrated was taken from the abdomen in the region of the groin when the eruption was at an acute oozing phase one year from the establishment of the eruption over the entire body. The epidermis is fragmented, there cellular degeneration, and small imperfectly formed vesicles are present in the rete. There direct communication between the overlying mass of dried exudate and the tip of the central oedematous papilla. Lymphocytes are scattered throughout the lesion, but polymorphs are practically absent.

Hæmalum and Eosin × 300



FIG. 88

Flexural Infective Eczema.—Showing similar changes to those in Figs. 81 and 83. The exudate in he dermal papillæ well shown and at one point there is break through the epidermis and continuity with the exudate on the surface.

Hæmalum and Eosin 100

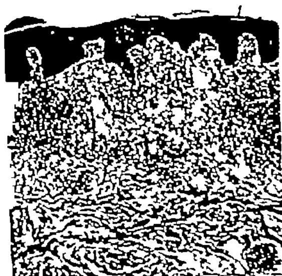


FIG. 89

Generalised Exfoliative Eczema.—One year duration. The epidermis shows irregular acanthosis with broadening of the rete pegs and parakeratosis. There is oedema of the papillary layer of the dermis, together with vascular dilatation and uniform and moderately dense infiltration by lymphocytes. The papillae are dome shaped and few lymphocytes are invading the epidermis. Compare with Psoriasis, and generalisation of flexural infective eczema (Figs. 55 & 81-88).

Haemalum and Eosin × 75.

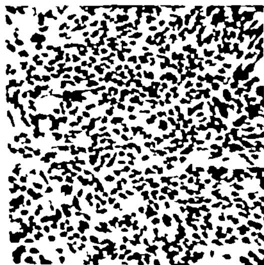


FIG. 90

Generalised Exfoliative Eczema.—The infiltration of the dermis almost entirely lymphocytic.

Haemalum and Eosin × 330.

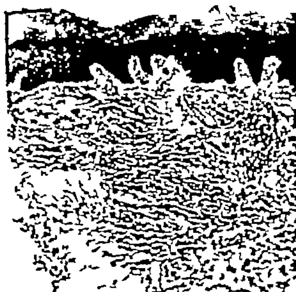


FIG. 91

Besnier's Prurigo.—The lichenified tissue is from the elbow fold in case of Besnier's Prurigo during remission. There is marked hyperkeratosis, some degree of acanthosis, and slight perivascular lymphocytic infiltrate.

Hæmatoxylin and Eosin × 75

CHEIROPOMPHOLYX

This term, and also that of Dyshydrosis, is used to indicate a vesiculo-bullous eruption affecting the palms of the hands, the sides of the fingers, and the soles of the feet. The eruption is of sudden onset, and in some cases has a tendency to recurrence. It was originally regarded as an affection of the sweat glands, but this view is not supported either by clinical observation or histopathological study. The microscopic appearances are those of the eczema reaction as it is evoked by chemical irritation, the fact that the process of vesiculation takes place in an epidermis with a specially well-developed stratum corneum ensuring the formation of structurally intact vesicles (Fig 92). From the etiological standpoint the condition is in the majority of cases attributable either to chemical irritation, to a fungus infection, or to the irritant action of noxious substances reaching the skin from within, e.g., toxins absorbed from areas of fungus infection in other parts of the skin surface, or from areas of focal sepsis of bacterial origin.



Fig. 92

Cheiropompholyx.—The structural changes are those of the eczema reaction as it evoked by chemical irritant
Hamilton and Evans × 65

PRIMARY VESICULO-BULLOUS ERUPTIONS OF INTERNAL TOXIC ORIGIN

This group of diseases includes Herpes Zoster Varicella, and Variola Erythema Multiforme, Dermatitis Herpetiformis, Pemphigus Vulgaris, and the Senear Usher syndrome and Keratodermia Blennorrhagica. The eruptions which depend on cutaneous idiosyncrasy to ingested drugs, particularly iodides, may occasionally present a primary bullous character but the effect of these drugs is erratic, and the eruptions which they produce do not constitute specific clinical entities. In addition, a variety of cutaneous disorders of internal origin, which are not primarily bullous, may from time to time develop bullae as a secondary phenomenon—e.g., urticaria and lichen planus.

In those diseases which are vesiculo-bullous from their onset it seems that the toxin or virus which produces them has a destructive action on the cells of the rete, causing them to become hydropic and vacuolated, and bringing about degenerative changes in the nuclei. These changes may even proceed to a stage of coagulative necrosis. The lesions which result from this action are characteristic for the various diseases as regards their clinical appearance and course, but microscopically the distinction is less clear cut, and they are to be differentiated more by the degree or stage of the degenerative process than by any specific or outstanding difference in the general effect of the causative agent on the cells of the rete, or in the type of vascular and cellular response which it may elicit in the dermis.

Herpes Zoster (Figs. 93-95) Preceding the development of intra-epidermic vesicles and bullae the rete cells undergo a series of degenerative processes. These consist in vacuolation, pyknosis and karyorrhexis, swelling of the cells, altered staining properties, and coalescence of degenerated cells with the formation of spaces or large multi-nucleated cells. Eosinophilic droplets may appear in the nuclei and in the cell cytoplasm. The degenerative process which affects the cells forming the base of the bulla may be so complete that its floor is ultimately formed by the bare dermis. In the bulla are to be found ballooned, multi-nucleated, and degenerated rete cells, floating free in the fluid contents. There is an intense leucocytic cellular reaction under the bulla, the inflammatory cells invade the rete, and the contents of the bulla may become purulent. There is vascular dilation and oedema in the dermis, where there may also be haemorrhage and necrosis. The lesion heals with the formation of a scar which may be depressed below the surrounding skin surface if necrosis, apart from epidermal degeneration, has been a marked feature

VARICELLA (Figs 96-99). The lesions in this disease are identical with those of herpes zoster The vesicles and bullae are more frequently confined to an intra-epidermal situation. Swollen and multinucleated cells are present in the base of the blister and in its contained fluid vacuolation is of frequent occurrence, and hyaline eosinophilic intra-nuclear bodies may be seen.

VARIOLA AND VACCINIA (Figs. 100-103) In these closely allied lesions the degenerative epidermal changes are more intense than in herpes zoster and actual necrosis with complete epidermal destruction is a feature. The swollen and multinucleated rete cells which are common in herpes zoster and varicella are much more rarely seen in variola, and in the latter disease extra-nuclear eosinophilic droplets (Guarnieri bodies) are to be found *in the cell cytoplasm* in contrast to similar structures situated *within the nuclei* in herpes zoster and varicella.

ERYTHEMA MULTIFORME (Figs. 104-106) In this disease the histological features are mainly centred in the epidermis. Over a circumscribed area, corresponding to the size and shape of the clinical erythemato-bullous plaques, the epidermis is honeycombed with fluid containing spaces of varying dimensions, the whole rete being thus disorganised by a series of multilocular bullae. The walls of these lacunae are formed by oedematous and partially degenerated rete cells, and the partitions between them may consist of little more than a thin strand of epidermis. The stratum corneum is intact. In addition to this inter and intra-cellular oedema the entire affected epidermis with the exception of its rete pegs, may be raised from the dermis by an exudate of plasma in which may be found strands of degenerated rete-cells, a few lymphocytes and leucocytes. Associated with this severe epidermal upset there is a remarkably slight inflammatory reaction in the papillary layer of the dermis, with a scanty perivascular infiltration of lymphocytes, and slight vaso-dilatation. It seems as if some unknown agent has exerted a profound toxic action on the rete, and that the vascular response to this has been almost exclusively one of increased capillary filtration the oedematous fluid being localised throughout the deepest layers of the rete with the production of a bulla, the roof of which is formed by almost the entire thickness of a disorganised rete. The epidermal necrosis in this disease has features in common with that seen in variola, and varicella.

DERMATITIS HERPETIFORMIS (Fig 107). The lesions in this eruption may be purely erythematous, urticarial, bullous, or a mixture of all three types Scarring is a common sequel in the bullous lesions due to the fact that they are frequently in a sub-epidermic situation. The cellular reaction in the dermis is lymphocytic in type, but there are a varying number of polymorphs present in the tissue forming the base of the bullae The blood shows a moderate eosinophilia, and eosinophils may be present in the bulla fluid. In addition to scarring the lesions

may cause hyperpigmentation, and melanophores may be seen in numbers in the dermis.

PEMPHIGUS VULGARIS (Figs. 108 and 109). The bullae are situated in the middle and deep zones of the epidermis, and in some cases they are practically sub-epidermal. They are generally unilocular and isolated rete cells in their walls and base may be vacuolated and ballooned, and some may have coalesced to form multi-nucleated cells. Even when Nikolski's sign is present (friability of the apparently intact epidermis in the vicinity of bullae, and the ability to make the bullae travel along the epidermis by pressing on their sides), there is no visible lack of cohesion in the surrounding rete beyond perhaps a slight degree of inter cellular oedema in the immediate vicinity of the bulla. A moderate cellular infiltration is present in the oedematous papillary layer of the dermis underneath the bulla leucocytes predominate, while in the perivascular areas the infiltration is composed of lymphocytes. In the vegetating variety of pemphigus vulgaris (pemphigus vegetans) verrucous excrescences develop from the exposed bases of the ruptured bullae, and the cellular infiltration in the dermis is more intense. In pemphigus the blood shows a marked eosinophilia.

SENEAR USHER SYNDROME (Figs. 110 and 111). This condition is a rare complication of lupus erythematosus and in its clinical manifestations it bears some resemblance to pemphigus. It is also referred to as pemphigus foliaceus. The bullae are so superficially placed in the epidermis that the roof is soon ruptured and remains as a flaccid epidermal tag. The shape of the lesion is usually that of a crescent. Histologically the bullae are seen to develop immediately below the stratum corneum and after rupture has taken place the exposed surface of the rete is ragged and eroded The epidermis is acanthotic and here and there the rete cells are oedematous, otherwise its structure is normal. There is a slight inflammatory reaction in the papillary layer of the dermis.

KERATODERMIA BLENNHORRHAGICA (Figs. 112 116). This eruption occurs as a complication of gonorrhoea, is generally situated on the soles and palms, and is occasionally sparsely distributed on the legs, trunk and arms. The individual lesions last from three to ten weeks or longer They commence as vesicles which become purulent and are transformed into an adherent crust. Their slow development and regression can be traced histologically and the most striking features are a marked degree of acanthosis with elongation of the rete pegs, and an infiltration of polymorphs, histiocytes, and lymphocytes which traverse the rete to become incorporated in layers and clumps in the overlying crust. The crust is composed of fibrin and dried plasma, inflammatory cells and parakeratotic epidermal cells In the earlier stages vesiculation continues to take place beneath this crust, which thus becomes increasingly thickened. The papillary layer of the dermis is grossly oedematous.

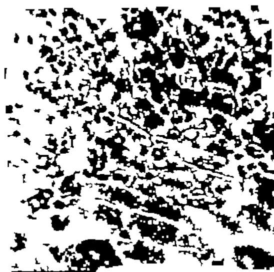


Fig 95

Herpes Zoster—Floating free in the bulla fluid are lymphocytes, swollen rete cells in various stages of degeneration multinucleated rete cells, and fragments of nuclei

Hamaker and Eaton 340



Fig. 96

Varicella.—Early papulo-vesicular stage. There are several large unilocular vesicles situated immediately under the stratum corneum. These collections of fluid rest on the entire thickness of the rete, the cells of which are undergoing disintegration and necrosis. The subjacent derma is edematous in its papillary portion, and in its deeper layers there is a moderate perivascular lymphocytic infiltration. *[illegible] and [illegible]* 65



Fig. 97

Varicella.—Early papulo-vesicular stage. Oedema fluid has collected beneath the stratum corneum to form large vesicles. The cells of the underlying rete are degenerated in varying degrees. They stain poorly, the intercellular bridges are no longer present, and in many instances the cell membranes have disappeared. The nuclear chromatin is lost, and the nuclei are represented by their membranes and nucleoli. In places the cell membranes and nuclei have disappeared entirely and the space is filled by a mass of poorly staining cytoplasm. *[illegible] and [illegible]* 22[illegible]



FIG 98

Varicella—Pustular stage Except at the edge of the lesion the entire rete is replaced by pool of fluid, presumably composed of oedema fluid and liquefied rete cells. The roof of this bulla is formed by the stratum corneum and in the deeper areas there is mass of nuclear debris, lymphocytes, and an occasional polymorph and histiocyte. The epidermal necrosis is sharply demarcated from the adjacent rete. The papillary layer of the dermis at the edge of the necrotic area the seat of lymphocytic infiltration.
Hamilton and Evans 65



FIG 99

Varicella—Pustular stage.—T the right of the section the rete cells and their nuclei stain poorly and the cell outlines are ill-defined. Here and there cells which have undergone an eosinophilic degeneration are to be seen surrounded by clear spaces. T the left, the rete cells have disappeared, their place being taken in the superficial area by homogeneous eosinophilic fluid roofed by the stratum corneum and in the deeper area the fluid contains large amount of nuclear debris and few lymphocytes. Here and there balloon cells can be distinguished in the superficial area of the bulla.
Hamilton and Evans 225

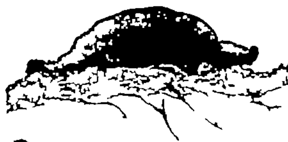


FIG. 100

Vaccinia.—The lesion is clearly demarcated from the surrounding skin. The surface consists of an exudate of coagulated plasma, and beneath this the epidermis is completely necrotic and infiltrated by inflammatory cells.
Hæmatoxylin and Eosin. 7



FIG. 101

Vaccinia. Edge of lesion.—The adjacent epidermis is acanthotic and the cells are swollen, stain poorly, and many are vacuolated. The lesion consists of dried serum in its upper portion, with necrotic epidermis in the deeper areas, the entire mass being infiltrated by inflammatory cells. The papillæ are œdematous and infiltrated by lymphocytes and polymorphs.
Hæmatoxylin and Eosin. 60



FIG. 102.

Generalised Vaccinia, pustular stage.—The surface of the lesion composed of mass of vacuolated and completely degenerated rete cells, invaded by polymorphs. Several small dried up vesicles are embedded in this mass. The underlying rete is acanthotic, and contains vacuolated cells, and cells which have degenerated to form homogeneous areas. The papillæ are oedematous, and both they and the adjacent dermis contain dense infiltration of polymorphs and mononuclears. *Hæmalum and Eosin.* × 75.



FIG. 103.

Generalised Vaccinia, pustular stage.—The rete is in state of extreme degeneration. The majority of the cells are vacuolated, some have lost their nuclei, the remaining cytoplasm glassy and stains poorly; the prickles are absent, and the degenerating cells appear to be coalescing. The papillæ are oedematous and packed with inflammatory cells. *Hæmalum and Eosin.* × 350.



Fig. 104

Erythema Multiforme.—An intense exudative process has developed in association with necrotic changes in the epidermis. The epidermis is honeycombed with fluid accumulations of varying sizes, and, with the exception of the rete pegs, it forms a roof for large bullæ, the base of which is formed by the papillary layer of the dermis almost throughout its entire extent.
Hamsden and Evans × 17



Fig. 105

Erythema Multiforme.—The bulla is almost entirely sub-epidermic, and the cells in the epidermis forming its roof have undergone degenerative and necrotic changes. The vascular and cellular reaction in the dermis forming the base of the bulla is exceedingly slight.
Hamsden and Evans × 100



FIG. 106

Erythema Multiforme.—The degenerative changes in the epidermis are sharply defined from the adjacent normal rete. The epidermis is honeycombed [illegible]th multi-locular vesicles, and forms the roof of [illegible] sub-epidermic bulla. There is [illegible] slight perivascular infiltration by lymphocytes.
Hæmalum and Eosin ×70



Fig. 107

Dermatitis Herpetiformis.—The section shows sub-epidermic bulla. The roof composed of the entire thickness of the epidermis, hich has been raised from the dermis by collection of fluid at the dermo-epidermic junction. The bare surface of the dermis forms the base, and on it there narrow band of lymphocytic infiltration. Deeper in the dermis there perivascular lymphocytic infiltration.
Hewitson and Lowe 43

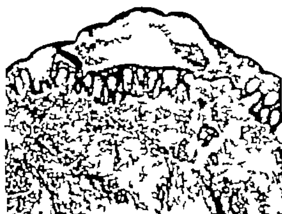


FIG. 108

Pemphigus Vulgaris.—A bulla has formed in the middle portion of the rete. There is some acanthosis. A moderate lymphocytic reaction is present in the underlying dermis. The epidermis surrounding the bulla appears to be normally constituted and there is no apparent lack of cohesion of the cells. Nikolsky's sign was not uniformly present in this case.

Hematoxylin and Eosin × 20



FIG. 109

Pemphigus Vulgaris.—In this example the bulla is almost sub-epidermal in situation. The cellular reaction is minimal. Nikolsky's sign could be easily elicited in this case.

Hematoxylin and Eosin × 15

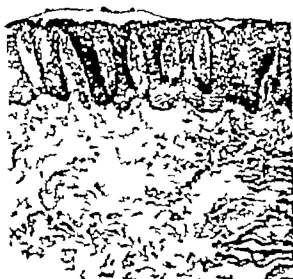


Fig. 110

Sennear Usher Syndrome.—The epidermis is acanthotic: the rete pegs are elongated, but the supra papillary portion of the rete is much reduced in width. The stratum granulosum is absent, and the thin stratum corneum is raised by a collection of fluid to form flaccid bulla. The papillæ are elongated, and there is a slight lymphocytic infiltration. The collagen fibres have a homogeneous glassy appearance. *Hæmalum and Eosin.* × 75.

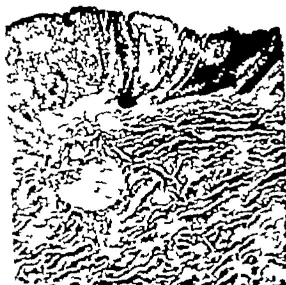


Fig. 111

Sennear Usher Syndrome.—The right half of the section shows the base of a ruptured bulla, the roof of which has disappeared. The rete and the papillæ are both slightly œdematous. The stratum granulosum has disappeared, and the exposed surface of the rete is ragged and fragmented. The collagen is somewhat glassy in appearance. *Hæmalum and Eosin.* × 75.



FIG. 112

Keratodermia Blennorrhagica, early pustular vesicular lesion.—The stratum corneum is intact and forms a covering to a mass of coagulated exudate in which are enmeshed numerous leucocytes and parakeratotic cells. The rete cells are oedematous, and leucocytes are present in the inter-cellular spaces. There is acanthosis. A leucocytic infiltration is present in the papillary layer of the dermis.
Haematoxylin and Eosin ×30.



FIG. 113

Keratodermia Blennorrhagica, an early pustular vesicular lesion.—A recent vesicle is seen resting on the rete and is surrounded by older coagulated exudate in which are numerous degenerated leucocytes. The rete cells are oedematous, and there is acanthosis with elongation of the rete pegs. The papillae are markedly oedematous.
Haematoxylin and Eosin ×75.

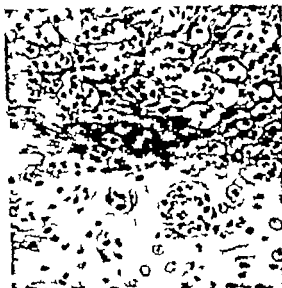


FIG. 114

Keratodermia Blennorrhagica.—This shows coagulated exudate infiltrated by leucocytes, resting on an oedematous rete. The rete is infiltrated by polymorphs, which at one point have collected to form small intra-epidermic abscess.

Hamilton and Evans × 350



FIG. 115

Keratodermia Blennorrhagica.—This section shows the marked degree of acanthosis and papillary oedema which is characteristic of the fully developed lesion. The stratum corneum has been lost, and squamous crust rests on the rete from which the stratum granulosum is absent.

Hamilton and Evans 50



FIG. 116

Keratodermia Blennorrhagica.—A lesion of longer standing showing a desiccating squamous crust. This is composed of alternating layers of coagulated exudate, collections of degenerated leucocytes, and parakeratotic cells. The stratum granulosum is absent. The acanthosis and papillary oedema are subsiding. There is a well marked lymphocytic infiltration in the papillary layer of the dermis.

Haemalum and Eosin × 80.

PRIMARY VESICULO-BULLOUS ERUPTIONS OF EXTERNAL ORIGIN

SCABIES (Figs 117 120) A vesicle in association with a burrow is the primary skin lesion of scabies. The vesicle often becomes purulent, and the scabies complicated by impetigo and furunculosis.

IMPETIGO CONTAGIOSA (Figs 121 123). A superficially placed intra-epidermal vesicle or bulla is the characteristic lesion of impetigo contagiosa. The roof of the vesicle is usually so thin that the lesion does not remain intact for long, and early rupture is the rule, except on the palms and soles where the stratum corneum is well developed. When the vesicle is preserved the contents, at first clear rapidly become purulent.

Histologically the early lesion consists of a collection of cell-free fluid underneath the stratum corneum. The rete which forms the sides and base of the vesicle shows no degenerative changes in its cells, and intercellular oedema is absent or scanty These is little or no oedema or cellular reaction in the papillary layer of the dermis. The process by which the bulla develops seems to be purely an exudative one depending on increased capillary filtration, and visible epidermal damage is of the slightest. (See vesicle formation in Eczema section).

While impetigo may be contracted through the contamination of any form of superficial injury there is a close association, particularly in children, between pediculosis capitis (Fig 125) with its attendant puncture wounds and excoriations, and impetigo of the scalp; and in adults, to a less extent, between impetigo of the body and pediculosis corporis (Fig. 124) and phthiriasis pubis (Fig. 128)

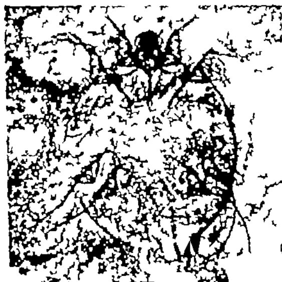


Fig. 117

Itch Mite—*Sarcoptes Scabiei. Adult female.*—Note the eight legs, with long hair-like processes.

Cleared Preparation 110



Fig. 118

Itch Mite—*Sarcoptes Scabiei.*—Embryo still enclosed in egg-case.

Cleared Preparation 350



FIG. 119

Itch Mite—Sarcoptes Scabiei.—Nymph or immature form, with six legs.

Cleared Preparation ×350



FIG. 120

Scabies. *A scabies burrow and the adjacent vesicle.*—The parasite has burrowed a cavity in the stratum corneum, and an egg is seen lying in this space. Immediately below and to the side of the burrow there is a large unilocular intra-epidermal vesicle the contents of which are slightly purulent. The base of the vesicle is formed by a thin layer of epidermal cells which are being invaded by polymorphs. There is slight vasodilatation and perivascular polymorph infiltration in the papillary layer of the dermis. A comparison between the size of the vesicle and the size and number of epidermal cells in its immediate neighbourhood suggests that in its formation there must have been a considerable loss of epidermal tissue in addition to a pushing apart of the cells in the area by an influx of capillary filtrate. (See 'formation of vesicles' in eczema section and Fig. 70).

Haemalum and Eosin ×80



Fig. 121

Impetigo Contagiosa.—A bulla has formed beneath the stratum corneum. The contents of the bulla are clear and cell free. The rete which forms its base is stretched and the pegs are absent. There is a slight degree of perivascular lymphocytic and leucocytic infiltration, and some separation of the collagen fibres.

Hæmatoxylin and Eosin × 70

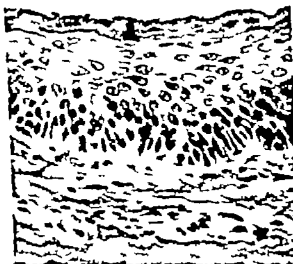


Fig. 122

Impetigo Contagiosa.—This shows the structure of the rete forming the base of the bulla. There is a slight degree of intercellular oedema and some of the cells stain rather faintly but on the whole the structure is compact and the tissue normal, and there is no evidence of the presence of capillary filtrate to account for the overlying bulla.

Hæmatoxylin and Eosin × 300



FIG 123

Impetigo Contagiosa.—This is an early stage of formation of bulla and appears as separation, by fluid, of the superficial cornified layers of the epidermis

Hematein and Eosin × 75

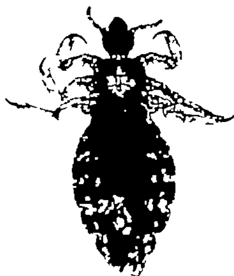


Fig. 124

Body Louse—Pediculus Corporis. Adult female.—The brownish-red colouration in the abdominal area represents the remains of ingested blood and has prevented the clearing of the louse during preparation.

Cleared Preparation × 14



Fig. 125

Head Louse—Pediculus Capitis. Adult male.

Cleared Preparation × 14.



FIG. 126 FIG. 127

FIG. 126.—*Nits of Head Louse attached to hair*
Cleared Preparation 14

FIG. 127.—*Nits of Head Louse attached to hair*.—An embryo present in one egg case. The other case is empty, the embryo having escaped
Cleared Preparation × 14



Fig 128

Crab or Pubic Louse—Phthirus inguinalis or pubis Adult
Cleared Preparation × 22

PUSTULAR ERUPTIONS

A variety of superficial inflammatory skin lesions may become purulent at some period in their evolution, and thus qualify to be included in the category of pustular eruptions. Lesions which are not primarily follicular pustules, but which may become purulent are the bullae and vesicles of impetigo contagiosum, all the varieties of herpes, pemphigus, dermatitis herpetiformis, eyrthema multiforme, the necrotic epidermal lesions of variola and varicella, the vesicles of scabies, and eczema, the papules of rosacea which become necrotic, and the papulo-necrotic tuberculides.

The term pustule should however be limited to those inflammatory lesions in which the reaction is from the start a polymorphonuclear leucocytic infiltration of the dermis and epidermis, and if this limitation is observed, it will be seen that the pustular eruptions are confined to superficial and deep inflammations of the hair follicles. The superficial pustule involves the ostium of the follicle, including the epidermis, and the reaction may extend downwards to include the sebaceous gland and the hair root. From the commencement of the reaction there is a brisk infiltration of polymorphonuclear leucocytes in these areas. The lesion is produced by the staphylococcus in all its varieties, and blockage of the ostium, or injury such as might be produced by avulsion of a hair or the lodgement of gritty particles or hydrocarbon products in the ostium, are predisposing factors for its development. Recurrent lesions are liable to develop as a result of autoinoculation of the organism, and pustulation is a common complication of a variety of superficial inflammations either because they lead to scratching and hence to abrasions, or because the staphylococcus finds their discharges a suitable medium for its multiplication and increase in virulence.

The true pustular diseases are SYCOSIS (Figs. 129-131), ACNE VULGARIS (Figs 133 and 134), FOLLICULITIS DECALVANS (Fig 132) and FURUNCULOSIS, and of course single non-recurrent pustules may develop on any area where the hair is strong. A pustule will not develop unless a hair is present in the follicle.

Cutaneous abscesses which simulate spontaneously-arising deep-seated staphylococcal follicular lesions may be caused by biting insects such as TICKS (Fig. 136) and JIGGERS (Fig. 135).

ORF—(Figs. 137 139). This lesion, which is primarily vesicular but which rapidly becomes purulent, occurs on exposed areas, and is usually single It appears to be contracted as a result of handling sheep suffering from pustular lesions in the region of the hoof In the human subject a secondary generalised eruption resembling erythema multiforme

may develop during the course of the primary lesion. Neither bacteriological nor serological examination, nor attempts at experimental inoculation have yielded any information as to the cause of the disease, but the presumption is that it is produced by the action of a virus.

The epidermis shows gross disorganisation. There is acanthosis, and large unilocular and multilocular bullae develop The cells of the rete forming the roof sides, and the base of this area are degenerated *They are swollen the prickles are lost, the cytoplasm is pale, the nuclei* stain poorly and may be pyknotic, hydropic vacuoles may be present, in some cells the nuclei have disappeared, the cell membranes are indistinct, and in places clumps of anuclear cells appear to have fused together to form homogeneous hyaline masses. Here and there eosinophil droplets are to be found in the cell bodies.

The papillae show an extreme degree of oedema and the lymph and blood vessels are dilated throughout the entire dermis, in which there is also a diffuse infiltration of inflammatory cells The lesion resembles those of variola and erythema multiforme, but necrosis is much less in evidence than in the former condition, and the cellular reaction in the dermis, and the epidermal degenerative changes are more marked than in the latter



Fig. 129

Staphylococcal Folliculitis (beard region).—This is commencing lesion, and oedema of the dermis surrounding the superficial portion of the follicle is more striking than the peri-follicular and perivascular infiltrate of leucocytes, which just commencing.

Hæmalum and Eosin × 65.



Fig. 130

Staphylococcal Folliculitis. Fully developed pustule (beard region).—A polymorphonuclear leucocytic reaction surrounds the follicle and most dense in its upper portion here the epidermis has been invaded.

Hæmalum and Eosin × 30

may develop during the course of the primary lesion Neither bacteriological nor serological examination, nor attempts at experimental inoculation have yielded any information as to the cause of the disease, but the presumption is that it is produced by the action of a virus.

The epidermis shows gross disorganisation. There is acanthosis, and large unilocular and multilocular bullae develop The cells of the rete forming the roof sides and the base of this area are degenerated They are swollen, the prickles are lost, the cytoplasm is pale, the nuclei stain poorly and may be pyknotic, hydropic vacuoles may be present, in some cells the nuclei have disappeared, the cell membranes are indistinct, and in places clumps of anuclear cells appear to have fused together to form homogeneous hyaline masses Here and there eosinophil droplets are to be found in the cell bodies.

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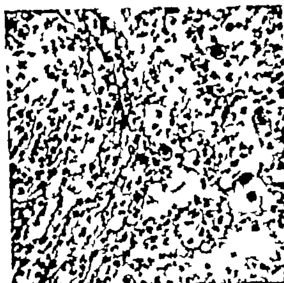


Fig. 131

Staphylococcal Folliculitis.—An area from Fig. 130 showing the dense polymorphonuclear infiltration, disintegrated epithelial cells, and edema.

Hematoxylin and Eosin. 375



Fig. 132

Folliculitis Decalvans.—There is a dense polymorphonuclear peri-follicular infiltration surrounding the entire length of the hair follicle which is destroyed by the process. In the adjacent dermis a perivascular leucocytic infiltration is present.

Hematoxylin and Eosin. 40



FIG. 133

Acne Vulgaris, Comedo stage.—This shows the incarcerated mass of horny cells and inspissated sebum plugging the orifice of a hair follicle. The follicular epithelium is thinned due to pressure. In the surrounding dermis the vessels are dilated and there are a number of lymphocytes scattered through it.
Haematoxylin and Eosin × 45.



FIG. 134

Pustular Acne.—A plugged follicle surrounded by a dense polymorphonuclear infiltration.
Haematoxylin and Eosin × 30.



FIG. 135
Jigger or Sand Flea—
Sarcopsylla (or Pulex) penetrans.
Cleared Preparation × 50.



FIG. 136
Tick—Dermacentor andersoni. Adult.
Cleared Preparation × 20



Fig. 137

Orf—Numerous multilocular and unilocular vesicles are present in the middle of the epidermis. The epidermis is disorganized and the individual cells are swollen and degenerated. There is marked papillary oedema and communicating channels exist between this oedematous area and the intra-epidermal collection of fluid. The dermis is oedematous and infiltrated by inflammatory cells.

Haemalum and Eosin × 15.



Fig. 138

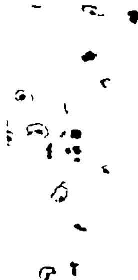


Fig. 139

Fig. 138.—*Orf*.—There are intra-epidermal and sub-epidermal collections of exudate, and they are intercommunicating. The epidermal cells are swollen and degenerated. There is diffuse cellular infiltration of polymorphs and lymphocytes in the dermis.

Haemalum and Eosin × 50.

Fig. 139.—*Orf*.—The prickle cells are swollen, the cytoplasm stains poorly, adjacent cells are coalescing and their cell membranes are indistinct; some are becoming completely disintegrated, and many are anuclear. Pyknosis is to be seen and in one cell three eosinophilic hyaline droplets are present in the cell cytoplasm.

Haemalum and Eosin × 450.

TINEA.

(Figs. 140-141.)

Tinea corporis lesions present a variable histological picture depending on the virulence of the fungus and the site affected. The changes range from a slight degree of simple inflammation, to vesiculation of the eczema type, and follicular pustulation comparable to that seen in sycosis.

In tinea kerion, in which the tissues have become allergic to the fungus toxin with the subsequent development of an immunity to the organism, there is a deepseated perifollicular reaction of granulomatous type, with lymphocytes, plasma cells, histiocytes, and an occasional giant cell. There may be some suppuration and as the reaction subsides scar tissue develops.



Fig. 140

Tinea Corporis.—Hyperkeratosis and parakeratosis are present, and there is some acanthosis which combined with papillary oedema and perivascular lymphocytic infiltration has flattened the rete pegs. The appearance is that of simple inflammation, and presents no individual features. *Hematoxylin and Eosin* × 66.



Fig. 141



Fig. 142

Fig. 141.—*Tinea Kerion.*—There is a deep seated and widespread perifollicular inflammatory reaction. *Hematoxylin and Eosin* × 33.

Fig. 142.—*Tinea Kerion.*—There is oedema and cellular infiltration composed of lymphocytes, a few histiocytes and an occasional polymorphonuclear leucocyte. *Hematoxylin and Eosin* × 330.

ROSACEA AND RHINOPHYMA.

(Fig. 143)

Although Rosacea is an erythemato-papular eruption and not a true primary pustular disease, the papules so frequently become necrotic and develop into virtual pustules that it may be most conveniently considered along with the pustular diseases.

In Rosacea there is a functional derangement of the cutaneous vessels of the face which is first noticed as frequent and repeated flushing of the cheeks, forehead, chin, and nose, and later by permanent dilatation of a number of these vessels. Associated with this vascular instability there is a tendency to the formation of indolent papules and pustules, and later a slow hypertrophy of the sebaceous glands may develop on the affected areas. The hypertrophy is most marked on the nose, where it may reach considerable proportions and form fleshy nodules. When the sebaceous gland hyperplasia has reached such a degree as to produce a noticeable tumour the clinical condition is known as Rhinophyma. The overgrowth of sebaceous gland tissue is a pure hyperplasia and is not adenomatous in character The inflammatory features of the disease are continued in the vicinity of the hyperplastic glands, and the repeated congestion associated with them predisposes to further glandular hyperplasia.

GRANULOMA PYOGENICUM.

(Fig 144)

This condition is essentially a hypertrophy of granulation tissue following injury usually a superficial puncture wound The granulation tissue has an epidermal covering which may be acanthotic in some places, and exceedingly thin in others. The newly formed fibrous structure contains numerous capillaries, fibroblasts, and histiocytes, and lymphocytes are abundantly scattered throughout.



FIG. 143

Rosacea and Rhinophyma.—This section shows hypertrophy and hyperplasia of the sebaceous glands. The gland structure normal and there no evidence of capsule. The lesion is hyperplastic and not truly adenomatous. A chronic inflammatory reaction in progress in the immediate vicinity of sebaceous gland. (Compare with Naevus Sebaceus, Fig. 260.) *Hamilton and Evans* × 15



FIG. 144

Granuloma Pyogenicum.—The epidermis is acanthotic, and there some parakeratosis. The dermis contains many newly formed capillaries, and there are numerous histiocytes and lymphocytes scattered throughout the somewhat homogeneous collagen. *Hematoxylin and Eosin* ×60.

TRAUMATIC INJURIES AND THE EFFECTS OF STRESS

The initial effect of trauma on the skin is a variable degree of destruction of cutaneous tissue, the extent of which depends on the nature and severity of the causative agent which may also determine the occurrence of special sequelae. The common feature in all injuries is a simple inflammatory reaction, intensified if pyogenic infection has supervened, followed by the development of granulation tissue and finally scar tissue.

BURNS (Figs. 145 147). The lesions produced by burning range from a slight erythema to complete charring of the skin and subcutaneous tissues In scalding, e.g by water or steam, vesication may be a feature. The histological changes therefore, vary from slight oedema of the epidermis with congestion of the dermis and a minimal leucocytic infiltration, to gross necrosis of the whole skin. In the latter case the necrotic area becomes saturated with serous exudate and there is intense congestion and leucocytic infiltration beneath it (Fig. 147). Later as healing occurs a fibrous scar tissue develops, and in the more severe and deeper burns a hypertrophic scar or a keloid may be produced. Secondary infection of the devitalised tissue intensifies the inflammatory reaction and leads to excessive scarring.

WOUNDS (Figs. 148–150). In simple physical trauma the changes are those of simple inflammation and as healing occurs the amount of granulation tissue and subsequent scarring is determined by the degree of tissue destruction or of associated infection.

Foreign bodies may be driven into the wound and complicate the picture. Thus particles such as copying ink, iron, dust, or silica may be introduced, and foreign-body giant cells form around them. If the particles are abundant, and especially if they are insoluble or nearly so, they may remain in the tissues for long periods. Particles of silica excite considerable fibrosis in the surrounding tissues and may give rise to the formation of foreign body giant cells and nodules closely resembling the tubercles of tuberculosis Silica particles embedded in the dermis can usually be seen in the inflammatory or fibrous nodules which they excite they are doubly refractile and can be displayed by examination with polarised light. Iron particles (Figs. 148 and 149), may be recognised by their chemical reactions. Copying ink (Fig. 150), deserves special mention as its introduction into the tissues may cause considerable necrosis and an intense inflammatory reaction.

VARICOSE ULCER (Figs. 151 and 152). Varicosity of the cutaneous venules of the leg predisposes to the development of ulceration in the lower third of the limb This may be due to external injury of the poorly nourished tissue with subsequent necrosis due to mild infection,

or it may result from thrombosis. Whatever the mechanism a localised gangrene involving the entire skin and sometimes the subcutaneous tissue is the result. Ulceration may be accompanied, or preceded by eczema.

The Corn (Fig. 153) and Bunion (Figs. 154 and 155) are both reactions to long continued or intermittent stress. In the corn there is a localised dense hyperkeratosis which not only projects on to the surface, but presses on the underlying rete causing it to become thinned and stretched and to lose many of its pegs. The subjacent dermis shows a varying degree of chronic inflammatory reaction. The bunion shows an area of degenerated, glassy and swollen collagen fibres, surrounded by chronic inflammation and covered by a hyperkeratotic epidermis.

Scar and Keloid (Figs. 156 and 157). The scar which results from the organisation of granulation tissue presents a thinned, sometimes hyperkeratotic epidermis with a complete absence of rete pegs In the dermis the collagen fibres are increased in density and deficient in connective tissue cells, and the elastic fibres are entirely absent or much reduced in quantity although they tend to be concentrated in the immediately adjacent surrounding skin. Sweat glands, hair follicles and sebaceous glands are absent. In scars of recent origin there may be a varying amount of perivascular lymphocytic infiltration and an excess of swollen, cellular recently formed collagen. At this stage the scar may appear hypertrophic but the infiltration later disappears and the collagen contracts and ceases to be swollen. In some cases, however and for no known reason, the newly formed collagen and fibroblasts continue to develop A hypertrophic mass which may greatly exceed the area of the original injury and which shows no subsequent contraction is thus produced. This condition is known as Keloid, and from its microscopic appearance and its tendency to recur rence it bears some relationship to tumour formation.

Stump Neuroma (Fig. 158). The condition known as stump neuroma consists of a mass of scar tissue formed round the end of a divided nerve from which numerous nerve fibrils arise and ramify throughout the scar



Fig. 145

Burn, 2nd Degree.—The epidermis is destroyed and is represented by a coagulum of dead cells and tissue fluid. The superficial layers of the dermis are markedly oedematous.

Haemalum and Eosin × 16.



Fig. 146

Burn, 2nd Degree.—A higher power view of the edge of the burn shown in Fig. 145. Here the epidermis is present and a small blister is seen as an oval, pink area situated in its deeper layers.

Haemalum and Eosin × 50.



Fig. 147

Burn, 3rd Degree.—The epidermis is destroyed and replaced by coagulated exudate. The superficial part of the dermis is necrosed, and there is oedema which extends into the deeper part of the dermis. *Hematoxylin and Eosin* × 10.



Fig. 148

Wound due to iron filings driven into skin.—The wound has become chronic and iron pigment can be seen in the surface exudate and deep in the wound. There is considerable fibrosis around.

Hæmalum and Eosin × 8.



Fig. 149

The same wound as Fig. 148.—The section has been treated by HCl and Potassium ferrocyanide, which turns the iron deposit deep blue.

Prussian Blue Reaction counterstained Fuchsin × 8.

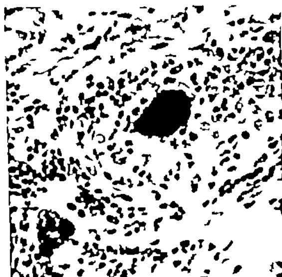


FIG. 150

Copying Ink deposit.—The particles of ink (accidentally introduced through the skin) lie in the dermis and are surrounded by large pale-staining histiocytes, some of which have fused around the larger deposits, forming "foreign body" giant cells. Scattered lymphocytes are present and towards the periphery there is a fibroblastic reaction.

Hamilton and Evans × 375.



FIG. 151

Varicose Ulcer.—The section shows an acanthotic epidermis which stops abruptly at the edge of the ulcer. The underlying dermis is slightly edematous, the vessels are dilated, and there is moderate leucocytic infiltration. Between the dermis proper and the purulent exudate on the left of the section which constitutes the surface of the ulcer, there is an area of recent granulation tissue containing numerous newly formed vessels and fibroblasts. *Hematoxylin and Eosin* × 15.



FIG. 152

Varicose Ulcer.—To the left of the section the epidermis is absent, there is purulent exudate in the upper portion and beneath this an area of recent granulation tissue. To the right of the section the epidermis is intact; the subjacent dermis is slightly edematous, more cellular than normal, its vessels are dilated, and there is moderate leucocytic infiltration. *Hematoxylin and Eosin* × 60.



Fig. 153

Clavus—"Corn."—From foot.—There is circumscribed excessive keratinization forming a mass of horny material which is pressed on to the underlying epidermis. This is hyperplastic but is stretched by the pressure of the horny mass.

Iron Hæmatoxylin and Van Gieson. ×24.



Fig. 154

Bunion of toe.—In the epidermis there is excessive cornification and thick rete malpighii. Immediately beneath are many dilated vessels. In the dermis is a large ill-defined mass of dense scar tissue composed of collagen the fibres of which run more or less in a concentric fashion. Many small blood vessels are present in the peripheral layers with collections of chronic inflammatory cells around them.

[illegible] 14

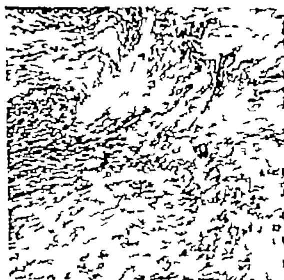


Fig. 155

Bunion of toe.—A higher power view of the margin of the fibrous mass, showing the collagen strands and several small vessels. The homogeneous area is the central part composed of more hyaline collagen, with few nuclei.

[illegible] 65

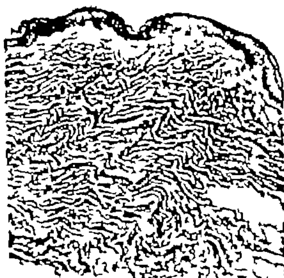


FIG. 156

An area of old scar tissue.—The epidermis is of normal thickness but the rete pegs are scanty and small. Underneath the epidermis there is a deep layer of more or less parallel wavy collagen fibres. The connective tissue cells are greatly reduced in number. There are few blood vessels, as the scar is old. Elastic tissue is absent.

Haematoxylin and Eosin × 60.



FIG. 157

A keloid.—This is an overgrowth of scar tissue, and consists of a great excess of collagen bundles with quite numerous fibroblasts and a few scattered lymphocytes.

Haematoxylin and Eosin × 60.



FIG 158

"Stump neuroma."—This is not true tumour as its current name suggests, but mass of scar tissue permeated by proliferating bundles of nerve fibres, stained black. It may form nodule of some size at the end of the severed nerve. The specimen is covered with thick layer of epidermis. This is an old lesion, showing few remaining blood vessels.
Holdell' Silver Method and Carmine ×35

The conditions included under this term have as their common feature a progressive hyperplasia of more or less undifferentiated mesenchymal cells. Actual tumour formation, with destruction and invasion of normal tissues, may also develop from these cells, giving rise to the various forms of reticulo- or reticulum-celled sarcoma.

The varieties of reticuloses were originally described in relation to certain hyperplastic changes in lymph glands, but the cells concerned have a wider distribution in the body. Normally they are found in the lymph glands, the spleen, and bone marrow where some of them form the reticulum or parenchyma, others are lining cells of the sinuses, and yet others are applied to the branching fibrils of the reticular framework of these tissues. They also occur as undifferentiated mesenchymal cells lying in the meshes of connective tissues, including the dermis. When they undergo hyperplasia they may form groups of individual polygonal cells, syncytial masses, or even giant cells, and they may also differentiate in various directions giving rise to histiocytes, fibrocytes, lymphocytes, and haemic cells, especially of the myeloid series. A single type or a mixture of these various cells may be found as the result of the hyper plastic process. Some of the cells produce fine argyrophil fibrils of reticulum.

A hyperplasia of the reticular cells and their derivatives may form part of a number of inflammations of known origin—e g. cutaneous tuberculosis—the process being referred to as an inflammatory reticulosis. A progressive hyperplasia may also occur as a result of unknown causes, as in certain "lymphadenopathies," and it is to this latter group that the term *Reticulosis* is restricted. The cutaneous manifestations of reti culosis are as follows — lymphadenoma cutis, mycosis fungoides, leukaemia cutis—the cells of the leukaemias representing hyperplastic derivatives of the undifferentiated marrow reticular cells, the monocytic variety being perhaps the most closely related to the original reticular cell—and reticulum-celled sarcoma.

In LYMPHADENOMA, or Hodgkin's disease (Figs. 159, 160 and 161), the superficial nodules have the same general characteristics as those in the lymph glands and spleen. There is a mixture of reticular cells, including histiocytes, recognisable as large polygonal cells with round or indented nuclei, giant cells (originally described by Greenfield and later by Sternberg and by Dorothy Reed), together with variable numbers of eosinophils and fibroblasts. A delicate fibrillary meshwork of argy rophil fibrils is present amongst the cells, and later it is replaced by collagen fibres.

Mycosis Fungoides (Figs 162, 163 and 164) also presents a variety of types of reticular cells which infiltrate and form masses in the superficial dermis. These cells comprise histiocytes, some of which are multinucleated, lymphocytes, and plasma cells, enmeshed in a fine reticulum.

Leukaemia (Figs. 165 166 and 167). Skin involvement is common in lymphatic and monocytic leukaemia, less so in the myeloid variety In all three varieties there is present in the upper and middle dermis an infiltration of cells which are more or less uniform in type and characteristic for the particular disease, and which have accumulated as a result of local hyperplasia, or by infiltration from the capillaries.

Reticulo-sarcoma (Figs 168–174) In this case the hyperplasia is malignant in character with invasion and destruction of the surrounding stroma and spreads by the blood stream and lymphatics. There is general uniformity in the type of cell present in a given tumour but any variant of reticular cell may be involved. A fine reticulum is usually present throughout the cell masses A sarcoma may arise primarily in the dermis, either from a single site or from several points simultaneously or metastases from a distant site may be widely deposited in the skin.



Fig. 159

Lymphadenoma (Hodgkin Disease).—Cutaneous nodule. From the under surface of the epidermis and extending throughout the entire dermis is a heavy infiltration by many cells amongst which can be distinguished several larger cells.

Haematoxylin and Eosin × 75.

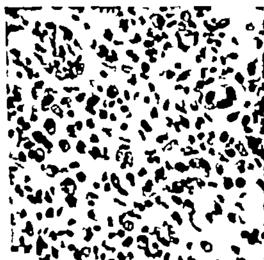


Fig. 160

Lymphadenoma.—This shows the cells of the nodule in detail. One of the large Hodgkin (so-called Dorothy Reed) cells is present near the margin; it is a small giant cell with several nuclei; many other histiocytic-type cells having large ovoid nuclei are distributed irregularly amongst many lymphocytes, plasma cells, and some eosinophils.

Haematoxylin and Eosin × 450.

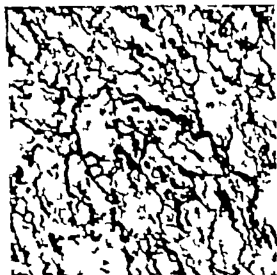


Fig. 161

Lymphadenoma.—A fine reticulum of delicate fibrils present between groups of the cells and even between and surrounding individual cells

Foot' Method, Counterstained Fuchsin × 475

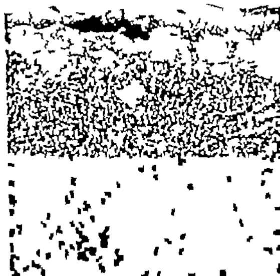


FIG. 162

Mycosis Fungoides.—In the dermis there is a dense infiltration with great numbers of cells of various types. Several small vessels run amongst the infiltrating cells.
Hæmalum and Eosin × 75.

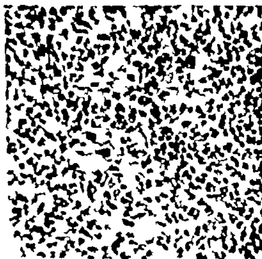


FIG. 163

Mycosis Fungoides.—*A portion of the nodule in more detail.* The cells are chiefly of the histiocytic type—large, polygonal, with rather faintly staining nuclei. Mingled with these are scattered lymphocytes.
Hæmalum and Eosin × 350.



FIG. 164

Mycosis Fungoides.—There is a reticulum in the form of fine dark threads intimately related to the cells.
Foot Method Counterstained Fuchsin × 400.



FIG. 165

Monocytic Leukaemia.—*Cutaneous nodule.* This general view shows the upper dermis extensively infiltrated with cells.

Haemalum and Eosin × 25.



FIG. 166

Monocytic Leukaemia.—*The same as Fig.* 165 to show the cellular infiltration partly in the meshes of the tissue of the dermis but more prominently in the vessels.

Haemalum and Eosin × 70.

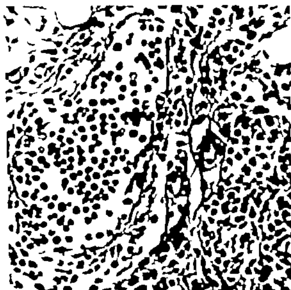


Fig. 167

Monocytic Leukaemia. The same as Fig. 165.—Here is shown a small blood vessel distended by great numbers of large monocytes and relatively few red corpuscles. Similar cells lie in the meshes of the adjacent connective tissue.
Haemalum and Eosin × 275.

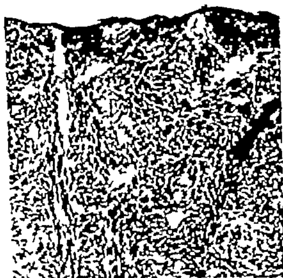


Fig. 168

Cutaneous Sarcoma, large spindle-celled type. From Forehead of an infant.—The tumour is composed of masses and strands of large spindle cells amongst which are several thin-walled, poorly supported blood vessels. The tumour cells have eroded through the epidermis.

[illegible] × 85.



Fig. 169

Cutaneous Sarcoma, large spindle-celled type. Same case as in Fig. 168.—This is a recurrence following removal of the original tumour. The cells have the same characters and are infiltrating widely into the epidermis and dermis; the margin is poorly defined.

[illegible] × 45.



Fig. 170

Cutaneous Sarcoma, large spindle-celled type. From same case as Figs. 168 & 169.—The reticulum is stained and appears as coarse filaments between groups of the large spindle cells and as finer threads between individual cells, though some cells show no reticulum around them.

Foot's Method, Counterstained Fuchsin ×475.

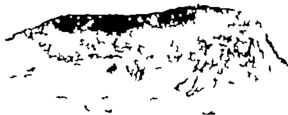


Fig. 171

Cutaneous Metastases of Sarcoma.—This view merely shows the general cellular nature of the tumour back infiltrating the dermis and stretching the epidermis. The margin is ill defined.

Hæmatoxylin and Eosin 8.

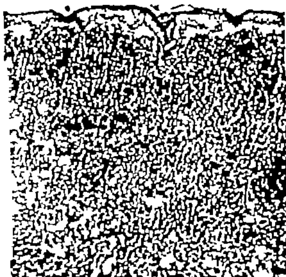


Fig. 172

Cutaneous Metastases of Sarcoma. Same as *Fig.* 171.—The cellular character of the nodule better seen here, the normal dermis being quite obscured and replaced by the tumour tissue.

Hæmatoxylin Eosin 70

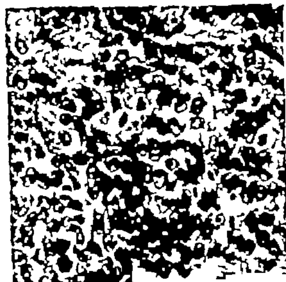


Fig. 173

Cutaneous Metastasis of Sarcoma. Same as Fig. 171.—The cells are all large, rounded or polyhedral in shape, with large pale-staining ovoid nuclei; several mitoses are seen. This shows the sarcoma merely as round-celled type.

Hematoxylin and Eosin. × 450

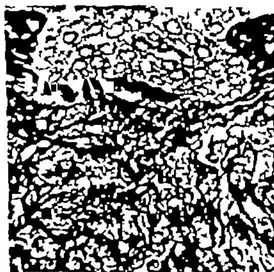


Fig. 174

Cutaneous Metastasis of Sarcoma. Same as Fig. 171.—With this staining method there is seen diffuse formation of reticulum fibrils around the cells of the tumour indicating its character as reticulum-celled sarcoma.

Foot Method Counterstained Fuchsin. 475

GRANULOMATOUS CONDITIONS

Under this heading are included and illustrated the following — syphilis lupus, tuberculides and sarcoid actinomycosis cutaneous Leishmaniasis (oriental sore). They all have the common feature of a cellular infiltration of the tissues by the various types of inflammatory cells and the *formation of granulation tissue, often in excessive amount*, with the final development of fibrosis. While the histological picture may be characteristic, e.g. in lupus, a closely similar appearance may be presented by syphilis Frequently it is necessary to have some confirmatory evidence, such as is given by special staining methods, to demonstrate the causal organism, before a positive diagnosis can be made.

Syphilis. The various cutaneous manifestations of syphilis all have the same general type of histological picture varying only in the amount of oedema or cellular infiltration which is present. This applies especially to the primary and secondary types of lesion. The tertiary lesion, e.g the gumma, presents a much greater degree of fibroblastic proliferation, often with necrosis in its centre, but the vascular changes and cellular infiltration are similar to those of the other stages.

The Primary Chancre (Figs. 175 178) shows a dense infiltration of the superficial dermis by mononuclear cells, largely composed of plasma cells along with a variable number of histiocytes and lymphocytes. The capillary vessels are increased in number they may exhibit endothelial swelling and proliferation, and are often surrounded by a collar of these infiltrating cells (Fig. 178). The epidermis is oedematous, infiltrated by mononuclears, and in due course ulcerates. Spirochaetes are present in great numbers in this lesion, or in a smear made from it, but they are only demonstrable by special staining methods (Figs. 179 and 180).

In the *Papulo-squamous* (Fig 181), and *Condylomatous Lesions* (Fig. 182), the above features are present in varying degree. The condyloma is a papulo-squamous lesion in which an epidermal hyperplasia has occurred on account of the moist situation of the lesion. In the later manifestations, the *Nodulo-cutaneous* syphilide (Figs. 183 186), and the *Gumma* (Figs. 187 189), there is fibroblastic proliferation as well as cellular infiltration in the nodules, and the inflammatory process extends more deeply and widely in the dermis. In these late lesions spirochaetes are scanty or absent.

When the different cutaneous manifestations of syphilitic infection are examined as a whole and contrasted one with the other it will be seen that the cellular reaction evoked during the active phases is essentially uniform, and differs only in the amount and depth of the infiltration, and not in the type of cell. The clinical lesions characteristic of the various

stages of the infection differ from each other much more obviously than do the histological findings. These variations in the distribution, configuration, and depth of the successive eruptive elements, together with the intervening periods of quiescence, suggest that throughout the course of the disease there is a progressive modification in the immunological and allergic processes stimulated by the infection.

LUPUS (Figs. 190-193) This is a definite tuberculous lesion which is characterised by typical tubercles, with "endotheloid" cells and giant cells, which coalesce and are diffusely distributed throughout the superficial dermis. Caseation is seldom a prominent feature. There is considerable fibroblastic reaction around the tubercles, the amount depending on the age and activity of the lesion. In the verrucose form there is marked hyperplasia and hyperkeratosis of the epidermis. Ulceration of the surface may occur either as a result of secondary pyogenic infection of the surface, or following necrosis of underlying cartilage, e.g. of the nose, which has become invaded by the tuberculous process.

TUBERCULIDES (Figs 194 and 195), have similar histological features to those of lupus, but in them the tubercles are smaller and much more discrete and clearly demarcated from the surrounding dermis, in which they are deeply placed.

In the papulo-necrotic form necrosis of the tissue overlying the inflammatory nodules is prone to occur with the formation of superficial ulcers.

SARCOID (Figs 196 and 197) The histological picture in the various clinical types of sarcoid is essentially that of a tuberculous process. The infiltration is circumscribed, it is deeply situated in the dermis, and caseation is absent.

Lupus, the tuberculides, and sarcoid are histologically very similar varying in degree rather than in kind and tubercle bacilli are rarely demonstrable even in a frank lupus. Sensitivity to tuberculin varies in the three groups, lupus cases showing a higher percentage of positives than "normal," the tuberculides a slightly lower percentage, and the sarcoid group a very low rate. It may be that variations in sensitivity to tuberculin account for the clinical and histological variations in the three conditions.

LEPROSY (Figs. 198-201) The cutaneous nodules are formed by a heavy infiltration of the dermis by large mononuclear cells (histiocytes) many of which are filled with Lepra bacilli, demonstrable by a modified Ziehl Neelsen staining (Fig. 201). There is also some fibroblastic proliferation and oedema, and later fibrosis occurs. Necrosis in the infiltrated area may lead to ulceration. Sometimes these cellular infiltrations are present along small superficial nerve bundles (Fig 198), a distribution which is also seen in the deep nerves in the anaesthetic form of leprosy

ACTINOMYCOSIS (Figs. 202 and 203) In the skin this usually takes the form of a sinus leading from an subjacent focus. The sinus is lined by granulation tissue, which at the orifice is covered with epithelium. Pus lies in the lumen of the sinus or covers its walls, and in it are found the felted masses of the mycelium of Streptothrix Actinomyces, stainable by Gram's method (Fig. 203). The lesion is that of a chronic inflammation and only the finding of the causal organism gives the clue to the diagnosis.

CUTANEOUS LEISHMANIASIS (Figs. 205-210), occurs as a chronic indolent nodule or plaque in the skin, which may ulcerate, and which is caused by an infection of Leishman Donovan bodies. These may be found free or in mononuclear phagocytes in scrapings from, or in sections of the sore (Figs. 209 and 210) They are small binucleated bodies easily demonstrated by Leishman's or Giemsa's stains The lesion in the skin is chronic inflammatory without specific characters, sometimes even showing nodules simulating cellular tubercles (Fig 207). The disease is transmitted by the sandfly (Phlebotomus papatasii) (Fig. 204).

RHINOSCLEROMA (Fig. 211) is a chronic granulomatous and sclerosing condition which affects the nose and adjacent structures. Histologically a dense infiltration of plasma cells and large vacuolated histiocytes is present in the middle and lower dermis and may extend to involve the subcutaneous tissues. The short encapsulated bacillus of rhinoscleroma is present in clumps within the large histiocytes, and it can easily be demonstrated in smears from the lesion.

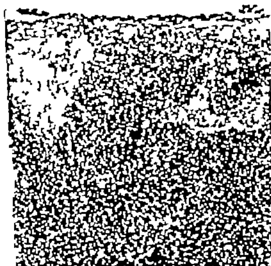


FIG. 175

Primary Syphilitic Sore (Chancre), general view of surface.—The epidermis, which is still intact though thinned, is being infiltrated by mononuclear cells. Such are present in great numbers diffusely throughout the dermis; amongst them run many capillaries.

Hæmalum and Eosin × 75

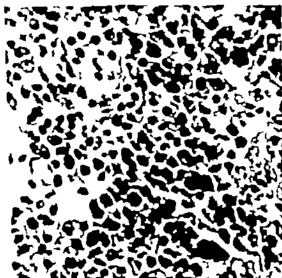


FIG. 176

Primary Sore. A portion of Fig. 175 to show details of cells.—There [illegible] mixture [illegible] various mononuclear types. Plasma cells with eccentric deeply-staining nuclei are numerous; amongst them are polygonal leucocytes with round or oval pale-staining nuclei; lymphocytes, with small dark nuclei, and an occasional polymorph leucocyte complete the collection.

Hæmalum and Eosin × 500



Fig. 177

Primary Sore. A slightly older lesion.—The epidermis is ulcerated towards one side and infiltrated by mononuclear cells elsewhere. The infiltration of the dermis is not so dense as in Fig. 175, it is oedematous, and there are many small blood vessels surrounded by thick collar of mononuclear cells.

Hamilton and Eason × 75.



Fig. 178

Primary Sore, to show especially the small vessels.—Several of these are seen with their walls and the perivascular area infiltrated by mononuclear cells; there is also some swelling of the vascular endothelium. There is oedema of the adjacent stroma.

Hamilton and Eason × 130.

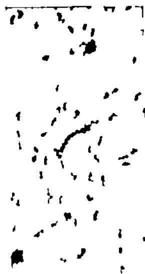


Fig. 179

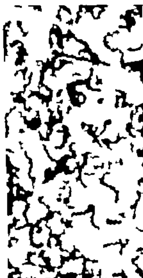


Fig. 180

Fig. 179. *Treponema Pallidum.*—The organism of syphilis as seen in a smear from a primary sore.
Stained by Fontana's method. × 1000.

Fig. 180. *Treponema Pallidum.*—As seen in the tissues.
Stained by Dobell's method. × 1000.



FIG. 181

Papulo-squamous Syphilide.—The infiltration of the dermis has the same characters as already described and shown in the primary sore (see Figs. 175 and 177), but the epidermis here intact and slightly hyperkeratotic.

Hamilton and Eason 75.



FIG. 182

Condyloma latum.—Condyloma latum is a papulo-squamous lesion which has become hypertrophied owing to its peri-anal, vulvar or scrotal site. There is much hyperplasia of the epidermis with exaggeration of the rete pegs. In the dermis is the same type of cellular infiltration as that seen in other cutaneous nodules (see Figs. 165 & 166).

Hamilton and Eason 55



Fig 183

Nodulo-cutaneous Syphilide with ulceration.—The infiltration of the dermis is similar to that described in Figs 175, 177 and 181 but the epidermis is invaded by the mononuclear infiltration and has ulcerated. There is hyperkeratosis merging with exudate from the ulcerated area. In the remaining part of the epidermis there is hyperplasia. *Haematoxylin and Eosin* × 75



Fig 184

Nodulo-cutaneous Syphilide.—A portion of the preceding figure (Fig 183) to show details of the cellular infiltration. The majority of the cells are plasma cells, intermingled with histiocytes, lymphocytes and an occasional polymorph leucocyte. Several capillary blood vessels are seen; they exhibit prominence of their endothelial cells and two contain many polymorph leucocytes in their lumen. *Haematoxylin and Eosin* × 350



Fig. 185

Nodulo-cutaneous Syphilide.—In this example the cellular infiltration is definitely aggregated around the small blood vessels both in the deeper parts of the dermis and in the papillæ. There is epidermal hyperplasia, with prolongation of the rete pegs and slight hyperkeratosis.

[illegible] and [illegible] × 70.

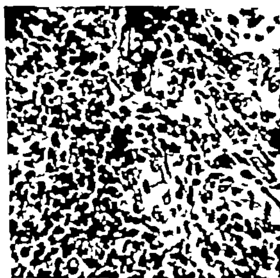


Fig. 186

Nodulo-cutaneous Syphilide, part of Fig. 185 to show details.—Several small vessels are shown: their endothelium is swollen and proliferated and there is a dense infiltration around them, the cells being mainly plasma cells and histiocytes.

[illegible] and [illegible] × 375.



FIG. 187

Gumma of skin, general view.—This shows merely an extensive infiltration of the dermis area by granulomatous nodules.

Henderson and Evans × 12.



FIG. 188

Gumma of skin. portion of the preceding figure, Fig. 187.—The dermis is heavily infiltrated with mononuclear cells, in places definitely aggregated around small blood vessels; there is also fibroblastic increase.

Henderson and Evans × 60.

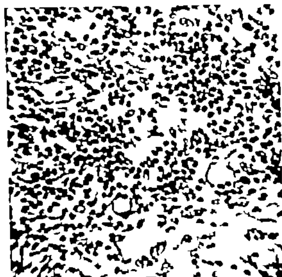


Fig. 189

Gumma of skin in more detail.—Several small vessels are seen, in some of which the lumen is almost obliterated by swelling and proliferation of the endothelium. Both in and around their walls there is an infiltration of mononuclear cells. A few fibroblasts are seen around the vessels and in the clearer areas.

Harrison and Evans 330



Fig. 190

Lupus Vulgaris.—There is slight hyperkeratosis with thinning of the epidermis and infiltration of it by lymphocytes. In the dermis there is diffuse infiltration by cells, mainly lymphocytes, and in its deeper area there are several tuberculous nodules composed of large pale-staining histiocytes (endothelioid cells).

Hematoxylin and Eosin 90



Fig. 191

Catarrhal Lupus. *A variant of Lupus Vulgaris.*—The tubercles and diffuse lymphocytic infiltration of the dermis are of the same character as those already described in Fig. 190. There is parakeratosis and also slight intercellular oedema of the epidermis.

Hematoxylin and Eosin 75



FIG. 192

Lupus Verrucosus. A variant of Lupus Vulgaris.—Here there is much hyperplasia of the epidermis with excessive keratosis. In the dermis the tuberculous lesion has the same general characters as in Fig. 190. In this specimen giant cells are numerous in the tuberculous nodules.
Hematoxylin and Eosin ×50



FIG. 193

Lupus Verrucosus. A portion of Fig. 192.—This is to show the details of the tuberculous nodule. Several giant cells are seen with surrounding histiocytes and lymphocytes.
Hematoxylin and Eosin ×275



Fig. 194

Papulo-Necrotic Tuberculide, from the hand, general view.—Scattered through the dermis and extending as deeply as the subcutaneous fat are granulomatous nodules which vary in size, and are clearly demarcated from the surrounding tissue.

Hæmalum and Eosin × 15.



Fig. 195

Tuberculide, more detailed view.—A typical giant cell is seen surrounded by number of histiocytes with lymphocytes further out.

Hæmalum and Eosin 225.



FIG. 196
Sarcoidosis, subcutaneous nodule.—Several granulomatous nodules, resembling tubercles, lie deep in the dermis.
[illegible] 45



FIG. 197
Sarcoidosis. To show details of the nodule.—This consists mainly of large histiocytes with an occasional small giant cell. Just around are scattered lymphocytes. The margin of the nodule clear cut. There no caseation. The lesion bears close resemblance to tuberculous nodule.
[illegible] 110.



FIG. 198

Leprosy, early tuberculoid form.—The granulomatous nodules follow the distribution of the small cutaneous nerves, one of which is seen cut obliquely in the lower left-hand corner. There is also a more diffuse infiltration extending along the line of the hair follicles to just beneath the epidermis.

Hematoxylin and Eosin ×65

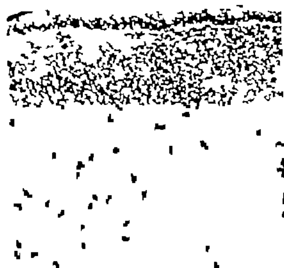


FIG. 199

Leprosy, cutaneous nodule.—The epidermis is stretched over an area of dermis which is heavily infiltrated by numerous inflammatory cells and granulomatous tissue.

Hematoxylin and Eosin ×80



Fig 200

Leprosy, high power, section of cutaneous nodule.—The infiltrate is seen to consist of great numbers of histiocytes and some fibroblasts forming a matrix in which run capillaries *Haematoxylin and Eosin* × 275

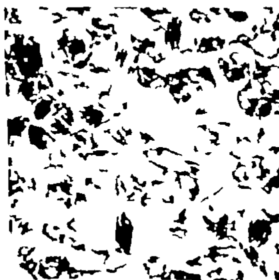


Fig 201

Leprosy.—To show the Lepra bacilli, stained red, some lying free, the majority packed within the large histiocytes ("Lepra cells")
Ziehl-Neelsen × 1000



FIG. 202

Actinomycosis.—*Portion of wall of sinus.* There is an epithelial lining and the cavity of the sinus full of pus cells and compact clump of the streptothrix actinomyces.
Haematoxylin and Eosin × 65

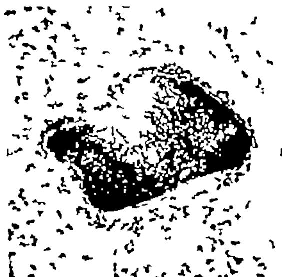


FIG. 203

Actinomycosis: same as Fig. 202.—Some of the contents from the sinus stained by Gram method, to show felted mass of the Gram positive filaments of streptothrix actinomyces surrounded by pus cells.
Gram Stain and Basic Fuchsin × 275

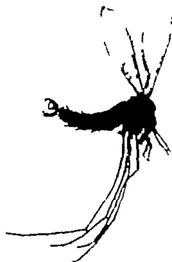


Fig. 204
Sand Fly—Phlebotomus papatasi
Stained Carmine × 11



Fig. 205
Cutaneous *Leishmaniasis* (Oriental Sore). *Early nodule.*—The dermis is heavily infiltrated by mononuclear cells of various types and the epidermis is becoming oedematous and disintegrated.
Haematoxylin and Eosin × 100



Fig. 206

Cutaneous *Leishmaniasis* (Oriental Sore) *Edge of Sore* —The epidermis is ulcerated away and the dermis is diffusely infiltrated by various types of mononuclear cells.

Haematoxylin and Eosin × 75



Fig. 207

Cutaneous *Leishmaniasis* (*Oriental Sore*) —Another portion which shows in addition to the diffuse cellular infiltration of the dermis, more localised nodules in which are a few giant cells, the whole resembling a tubercular nodule.

Haematoxylin and Eosin × 55

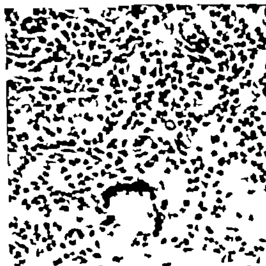


Fig. 208.

Cutaneous Leishmaniasis (*Oriental Sore*).—*The same as Fig.* 207.—A more detailed view of nodule showing to be composed of histiocytes, some lymphocytes and giant cell. *Hematoxylin and Eosin* × 375



Fig. 209



Fig. 210

Fig. 209.—Cutaneous *Leishmaniasis* (*Oriental Sore*).—In this the Leishman-Donovan bodies are stained and are seen to lie within the large histiocytes of the nodule. *Leishman Stain* 1,000

Fig. 210.—Cutaneous *Leishmaniasis* (*Oriental Sore*). *A smear from sore on the skin.*—One large mononuclear cell (histiocyte) seen with many Leishman-Donovan bodies in its cytoplasm. The bacilliform character of these bodies indicated.

Leishman Stain 1,000

NAEVUS

The scope of the term naevus is sometimes restricted to a variety of cutaneous tumour in which the predominating cell is the pigmented or potentially pigment-producing type known as the naevus cell, but as a number of other tumours which occur in the skin have certain features in common with this particular example, although differing from it histologically it has been thought more appropriate to give the term a wider meaning and to define it as follows — A naevus is a circumscribed hyperplasia or tumour formation which has its origin in aberrant embryological cutaneous structures or "rests." Naevi may be congenital or may appear at any age and are of almost universal occurrence. They develop slowly and sooner or later with few exceptions, reach a stationary stage. In rare cases they undergo malignant changes.

As naevi may develop from any one of the elements which are normal constituents of the skin, and as in some cases several types of cells or structures are involved, the naevi present great variations in their histological appearance. They may be classified as follows —

DERIVED FROM THE EPIDERMIS.	NAEVUS KERATOSUS. NAEVUS SENILIS. NAEVUS (EPITHELIOMA) CYLINDROMATOSUS (*Cylindroma*). NAEVUS PIGMENTOSUS.
DERIVED FROM THE EPIDERMAL APPENDAGES.	NAEVUS PILOSUS, AND PILONIDAL SINUS. NAEVUS (EPITHELIOMA), ADENOIDES CYSTICUM. NAEVUS SEBACEUS. NAEVUS SEBOCYSTOMATOSUS. NAEVUS SYRINGADENOMATOSUS (*Hydrocystoma*). NAEVUS SYRINGADENOMATOSUS PAPILLIFERUS.
DERIVED FROM COLLAGEN	NAEVUS FIBROMATOSUS.
DERIVED FROM VASO-FORMATIVE CELLS.	NAEVUS VASCULOSUS. LYMPHANGIOMA. HAEMANGIOMA. ANGIOKERATOMA. GLOMUS. ADENOMA SEBACEUM (PRINGLE).

NAEVUS KERATOSUS (Figs. 212 214). In this naevus the epidermis alone is involved, and the abnormality takes the form of an extreme degree of cornification. The thickened stratum corneum may simply form a compact mass which projects above the skin surface, or the epidermis may form a series of ridges between which the horny masses are embedded. The rete malpighii may be either acanthotic or diminished in thickness. The sweat and sebaceous glands in the area show no abnormality There may be a small amount of lymphocytic perivascular infiltration.

These naevi usually have a linear distribution and are referred to clinically as naevus linearis, naevus unius lateris, and ichthyosis hystrix. The excessive cornification gives them a darkish colour but there is no increase in melanin, and no naevus cells (see later) are present. The developmental abnormality may be confined to the mouths of a few adjacent hair follicles, and the name naevus acneiformis has been given to this type.

In the absence of any knowledge of the etiology of the conditions known as **Darier's Disease, Porokeratosis, and Acanthosis Nigricans**, and as they present clinical features as regards development and course which bear some similarity to the naevi, they are included along with the hyperkeratotic naevi to which they bear some histological resemblance.

Darier's Disease (Figs. 215 217). The lesions of this rare condition, which presents a striking clinical picture, are brought about by a process of dyskeratosis, a premature and abnormal keratinisation of individual rete cells. The process of abnormal keratinisation affects individual cells, or groups of cells, and this change is apparent even in the middle rete and more prominently in the stratum granulosum. The cells in question lose their prickles, become detached from their neighbours so that they come to lie in a small lacuna, the cell membrane becomes thickened, the nucleus is pyknotic, the cytoplasm assumes a homogeneous hyaline appearance, and vacuolation may be seen. These dyskeratotic cells (*corps ronds*) are gradually pushed up into the stratum corneum which is itself thickened and tends to become invaginated as horny plugs into the subjacent epidermis In this area of hyper keratosis the dyskeratotic cells may still be discernible, or they may be represented only by fragments of their pyknotic nuclei (*grains*), the cell body having merged with the surrounding normal keratohyalin. There is a moderate degree of acanthosis, and a tendency to the downwards development of narrow and pointed epidermal processes The epidermal proliferation never exceeds the bounds of an ordered hyperplasia, and malignancy has not been known to develop

Porokeratosis (Fig. 218) consists of a localised area of hyperkeratosis, which usually involves the orifice of a sweat-gland duct, and which projects on the surface as a horny spur These lesions are arranged in the form of a small circle, the original central area having become atrophic. The condition is often familial and hereditary and the lesions may assume a linear distribution.

Acanthosis Nigricans (Fig. 219) is a rare skin disease characterised histologically by hyperkeratosis and hyperpigmentation. As far as these features are concerned it bears a histopathological resemblance to naevus unius lateris. The disease may be naevoid in character—in some cases it is present at birth or appears early in life—and a familial tendency has been noted It is therefore convenient to place it along with the true hyperkeratotic naevi, if only for comparison. The chief

interest in acanthosis nigricans, which is benign as far as its cutaneous manifestations are concerned, is that visceral carcinoma is associated with some fifty per cent of cases.

Naevus Senilis (Figs. 220 and 221) This lesion is also known as verruca seborrhoeica and verruca senilis. It makes its appearance during or after middle age and consists of a flat brownish growth with an uneven fleshy surface which is usually covered with a pultaceous scale. It is frequently multiple, and occurs on the scalp, face and trunk. There is no evidence that it is allied to the contagious verrucae. On rare occasions it is the starting point of a squamous-cell carcinoma, but this occurs so seldom that it would be unjustifiable to place naevus senilis in the class of precancerous dermatoses

Naevus senilis consists of a hyperplasia of the rete, which takes the form of a network of almost uniform thickness throughout the lesion. There is no tendency to the formation of downward projecting epidermal processes such as is seen in verruca vulgaris, nor is there vacuolation of the rete cells, or the development of eosinophil droplets within the cell cytoplasm. The stratum corneum is thickened and from its under surface horny masses project into the underlying rete. These cornified masses may branch so that on section isolated plugs of stratum corneum may appear to be imbedded in the substance of the rete. The hyper keratosis gives a darkish colour to the clinical lesion, but there is no increase in the melanin content of the basal layer

Naevus (Epithelioma) Cylindromatosus (Fig. 222). This rare tumour also called cylindroma, is usually described along with basal cell carcinoma, although it shows no malignant tendencies of any kind. Its usual site is the scalp, where it occurs in varying numbers in an individual case, the lesions usually making their first appearance in childhood or adolescence. They vary in size from that of a pea to a tomato and tend to be somewhat pedunculated.

Histologically the tumour is composed of irregularly shaped masses of cells of basal type situated in the middle portion of the dermis On section these collections are circular oval, or bizarre-shaped. The cells are of two types, those at the periphery being smaller and more darkly staining than those in the centre. The cell masses are encircled by a band of homogeneous collagen, the same homogeneous material is present between the cells, and cavities of varying sizes are present in most of the cylindrical cell masses. The homogeneous encasing collagen does not exhibit the staining properties of hyaline degeneration, and it is regarded as a primitive form of collagen.

Naevus Pigmentosus (Figs 223 250). This variety of naevus is characterised by the presence of pigment-forming cells in the dermis. These cells are referred to as naevus cells, they contain the pigment forming oxydase and they are presumably of epidermal origin. They are quite distinct from the pigment-containing phagocytic wandering cells (melanophores) which are normally present in the dermis, and

which merely store and remove formed melanin but are incapable of producing it. The naevus cell is medium sized round oval, or polygonal in shape, and its nucleus is poor in chromatin. In the pigmented naevus these cells are present in varying numbers in the dermis. They are not distributed in any constant pattern, sometimes occurring as a dense mass, sometimes in columns set at right angles to the epidermis, and sometimes in small clumps. Their content of formed melanin is variable not infrequently they contain no melanin whatsoever and sometimes the basal cells of the epidermis are more highly pigmented than the subjacent naevus cells Larger polygonal melanophores may be present amongst, or in the vicinity of the naevus cell masses. The epidermis overlying the naevus cells may be normal in appearance or it may be acanthotic and hyperkeratotic.

In the *Blue naevus* (Figs. 239-241) the naevus cells and melanophores are deeply placed in the region of the coils of the sweat glands.

Pigmented naevi may develop malignant tendencies and when this occurs the degree of malignancy is extreme. Histologically the malignant pigmented naevus, or malignant melanoma (Figs 244, 245 and 247 250) as it is usually called, shows dense penetrating masses of naevus cells, which are irregular in shape and size and which show numerous mitoses There is a marked tendency for the malignant cells to penetrate the epidermis and appear in it as small clumps or nests The decision as to whether a naevus is benign or malignant may present considerable difficulty in the early stages of the change from one state to the other (Figs 242 and 243), and in some cases both types of growth are to be seen in a single tumour

Metastasis from a malignant melanoma takes place through the lymph channels and the blood stream, and the liver lungs and skin are frequent sites for the secondary growths. In the skin they frequently occur in showers, and spontaneous and complete regression of secondary skin growths has been noted. This appears to be brought about as a result of fatty degeneration of the tumour cells, the pigment being absorbed by histiocytes.

NAEVUS PILOSUS (Fig 251). In its simple form the naevus pilosus consists of a hyperplasia of hair follicles, mainly of the lanugo type. Surrounding the follicles there is a whorled agglomeration of collagen bundles and the intervening collagen is increased in amount and is more cellular than usual—in fact the mass may resemble a fibroma. The overlying epidermis is normal. These lesions usually occur on the face, and are particularly common in the region of the alae nasi, where they form rounded tumours, often with a slightly constricted base, which may reach half a centimetre or more in diameter

Hair follicles in abnormally large numbers may be present in a pigmented naevus, a mixed variety of naevus being formed—*naevus pigmentosus et pilosus*

The PILONIDAL SINUS (Figs. 252 254) arises in association with a localised hyperplasia of misplaced hair follicles—a developmental inclusion or rest—and it therefore falls into the category of naevus. The innumerable hair follicles are poorly developed and spring from the base and sides of a sinus which opens on to the surface. The upper portion of the sinus is lined with epidermal epithelium which is continuous with the adjacent surface epidermis. Infection of the sinus may take place with the production of an indolent subcutaneous abscess which tracks widely in the surrounding tissue and gives rise to multiple discharging sinuses The pilonidal sinus generally occurs over the lower sacral and coccygeal regions.

NAEVUS (EPITHELIOMA) ADENOIDES CYSTICUM (Figs. 255 and 256). This structure was originally described as epithelioma adenoides cysticum, but it is a benign type of tumour which shows no epitheliomatous tendencies. It occurs clinically as multiple pin-head to pea-sized tumours situated on the face and trunk. It usually becomes apparent during adolescence.

Histologically it is composed of numerous cystic spaces containing keratin material, situated in the upper and middle areas of the dermis The walls of these cysts have the structure of a hair follicle, and from the outer layer of cells on part of the circumference there arises a network of cellular strands. Similar strands may be seen projecting downwards from the basal layer of the overlaying epidermis which is stretched and somewhat thinned. The cells composing these networks have the appearance of basal cells, but once the lesion has developed the cells show no further tendency to invade the surrounding dermis, and the junction between their strands and the surrounding fibrous tissue is clear cut. The supporting tissue is more cellular than normal but there is no inflammatory cellular reaction such as is usually seen in basal cell carcinoma.

NAEVUS SEBACEUS (Figs. 257-264). Clinically naevus sebaceus takes the form of a linear lesion on the scalp, the supra- or retro-auricular region, the forehead, the cheek, or the neck. The lesion is usually present at birth and is by no means an uncommon one. The surface of the tumour is flat and only slightly raised above the surrounding skin. The tumour is formed by a mass of firm yellowish papules, which are frequently umbilicated.

Histologically this naevus is composed of numerous hypertrophic sebaceous glands which are of normal structure The ducts are dilated and are filled with sebaceous material and epidermal debris There is no capsule enclosing the area, and the lesion is a hyperplasia of the sebaceous glands and not an adenoma. The sweat glands in the area may show cystic dilation of their ducts and of the coil portion. The epidermis on the area involved in the sebaceous gland hyperplasia may be thin and stretched in places, and in others show an acanthosis similar to

that seen in naevus senilis A naevus sebaceus may in rare instances be the starting point for a carcinoma of either basal or squamous-cell type (*Figs.* 263 and 264)

NAEVUS SEBOCYSTOMATOSUS (Figs. 265 and 266). In some cases cystic dilation may affect large numbers of the sebaceous glands the condition being described as sebocystomatosis, or steatocystoma multiplex. The condition is often familial and should be considered as a naevoid type of cystic abnormality which does not result from obstruction to the sebaceous gland duct as in the case of the much more common sebaceous retention cyst. Apart from the absence of the plugged orifice the lesions of sebocystomatosis resemble those of the retention cyst and also milium lesions, although the latter are much more minute. In the example shown a cellular papilliferous process is present as an ingrowth from the cyst wall (naevus sebocystomatosus papilliferus).

NAEVUS SYRINGADENOMATOSUS (*Hydrocystoma*) (Figs. 267 and 268). The clinical appearance of this condition is that of a small somewhat translucent papule, and the lesions are usually multiple. The upper part of the trunk and face are the usual sites.

Histologically the tumour is composed of numerous dilated sweat gland ducts, which appear on section as cysts of varying sizes scattered profusely throughout the entire dermis.

There is a papilliferous variety—NAEVUS SYRINGADENOMATOSUS PAPILLIFERUS (Figs. 269-275)—which bears a close clinical resemblance to naevus sebaceus, and none to the simple syringadenomatosus variety It is usually found on the face, is often linear and in contrast to naevus sebaceus it not infrequently becomes eroded on the surface and presents a reddish moist appearance, resembling exuberant granulation tissue. The coiled secretory portion of the sweat duct may be normal in appearance or dilated. Above that level cystic dilations similar to those seen in naevus syringadenomatosus are to be seen and in the superficial zone of the dermis papillary growths project into the lumen of these cysts. *Finally a dilated duct opens on to the surface through a wide cup shaped* depression. This depression is lined with epithelium of sweat-gland duct type which is continuous at the periphery with the epidermis. Papillary processes rise from the floor of the depression and project towards the surface.

The cysts are lined by two layers of normal sweat-duct epithelial cells, and the papilliform projections consist of a fibrous tissue stroma covered by a similar layer of cells which is continuous with that lining the cyst. The fibrous tissue surrounding the cysts and composing the stroma of the papillary projections is densely packed with plasma cells. Some cysts are formed by dilatation of the coil portion of the sweat gland the epithelium of which is stretched and thinned.

In some cases there is a co-existing hyperplasia of sebaceous glands so that the lesion is a mixture of naevus sebaceus and naevus syringadenomatosus papilliferus



Fig. 212.

Naevus Unius Lateris.—There is a most marked degree of hyperkeratosis, the hypertrophied stratum corneum is in the main normal in structure but parakeratosis is present in places. The stratum granulosum is thickened. There is a considerable degree of acanthosis, but this is regular in character. The papillae are hypertrophied, and there is a small amount of perivascular lymphocyte infiltration. There are no naevus cells present.

Haemalum and Eosin × 18



Fig. 213.

Naevus Unius Lateris.—This is a higher magnification of Fig. 212 showing hyperkeratosis, acanthosis and hypertrophy of the papillae.

Haemalum and Eosin × 90



Fig. 214

Naevus Unius Lateris.—The hyperkeratosis does not protrude on to the surface so much as in Fig. 212. There is no acanthosis, the rete being thinned and stretched and the pegs few and far between. Sweat-gland ducts are seen in the stratum corneum of the naevus. There is little or no perivascular lymphocytic infiltration. Sebaceous glands are present and are normal in appearance.

Hæmalum and Eosin. 50



Fig. 215

Darier's Disease.—A horny plug invaginates the epidermis and in it are to be seen small granules of degenerated nuclei. The epidermis is acanthotic, and a group of dyskeratotic cells is seen lying in a clear space. There is some degree of lymphocytic infiltration in the subjacent dermis.

Haematoxylin and Eosin × 100



Fig. 216

Darier's Disease.—The horny plug contains keratinised dyskeratotic cells. One such cell is to be seen in the deeper part of the epidermis. There is acanthosis with the production of elongated downward projecting columns of epidermis. In spite of this apparent tendency for the epidermis to invade the dermis, Darier's disease does not develop malignant features.

Haematoxylin and Eosin × 275.



Fig. 217

Darier's Disease.—Dyskeratotic cells ("corps ronds") are to be seen just below the stratum granulosum. They are surrounded by clear space, and varying degrees of dyskeratotic changes are present. The cell membrane is thickened and vacuolation is present in one cell. In all of them the nucleus is pyknotic and the cytoplasm has a hyaline appearance. *Hematoxylin and Eosin* ×380.



Fig. 218

Porokeratosis.—There is marked hyperkeratosis and some parakeratosis forming a heaped-up mass at the mouth of a sweat-gland duct. The epidermis on which the spur is resting is normal in structure, but owing to its being stretched the rete pegs are absent. There is some small round-cell infiltration in the dermis underneath the horny spur.

Hamilton and Evans. 70.



FIG. 219

Acanthosis Nigricans.—There is excessive cornification on the surface. The epidermis is atrophic and reduced to only one or two layers of epithelial cells and there is disappearance of the rete pegs. There considerable amount of melanin pigment in the deepest layer of the epidermis, also some particles in the dermis. The dermis dense and its collagen is hyaline.

Haematoxylin Eosin 110



FIG. 220

Naevus Senilis. (*Seborrhoeic Wart*).—The main feature is irregular acanthosis, which forms a network. There is some hyperkeratosis, and horny plugs project downwards into the rete. The basal layer is normal and there is no increase in melanin. The dermo-epidermic junction is well defined.

Haemalum and Eosin × 12½



FIG. 221

Naevus Senilis. (*Seborrhoeic Wart*).—This shows an irregular reticulate acanthosis, with no tendency to downward projection of the rete pegs. The intrusion of horny plugs from the surface into the rete is seen. The basal layer shows no accumulation of melanin granules, the frequent dark colour of the lesions being due to the hyperkeratosis. The dermo-epidermic junction is clearly demarcated and there is the very slightest perivascular infiltration.

Haemalum and Eosin × 65



Fig. 222

Naevus Cylindromatosus.—The tumour is composed of masses and cords of epithelial cells similar to those seen in the basal-cell carcinoma, which it resembles. The cells of the peripheral layer are cubical to columnar in form. Several of the epithelial masses show cystic spaces within them. There is a well-defined supporting fibrous stroma. The epidermis is stretched out over the tumour but separated from it by a zone of fibrous tissue.

Haematoxylin and Eosin. × 65.

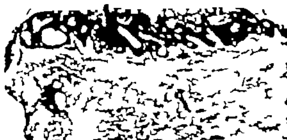


Fig. 223

Naevus Pigmentosus (Melanoma).—There is much acanthosis of the epidermis and the dermal papillae are seen cut in various planes amongst the epithelium. In these papillae are deposits of melanin pigment.

Haemalum and Eosin × 12



Fig. 224

Naevus Pigmentosus (Melanoma).—The same as Fig. 223, to show in more detail the pigment both in the dermal papillae and, to a lesser degree, in the basal cells of the epithelium. There is considerable lymphocytic infiltration around small vessels of the dermis.

Haemalum and Eosin 65.

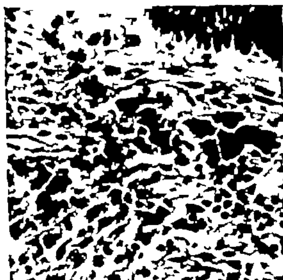


Fig. 225

Naevus Pigmentosus (Melanoma).—The same as Figs. 223 and 224 showing the melanin pigment packed into large cells of histiocytic type (melanophores) lying in the meshes of dermal papilla. Around are scattered few non-pigmented naevus cells, some lymphocytes and fibroblasts. A small part of the basal layer of the epidermis shows ith scanty pigment in some cells.

Haematoxylin and Eosin ×400.



Fig. 226

Naevus Pigmentosus (Melanoma).—This is papillomatous structure hich covered by thin layer of stretched epidermis. The matrix extensively occupied by masses of naevus cells amongst hich are specks of pigment.

Haematoxylin and Eosin ×9.



Fig. 227

Naevus Pigmentosus (Melanoma).—A portion of the same naevus as Fig. 226, to show the epidermis and the numerous columns of "naevus cells" occupying much of the connective tissue stroma.

Haemalum and Eosin × 90.

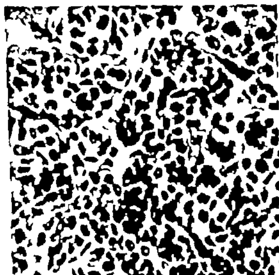


Fig. 228

Naevus Pigmentosus (Melanoma).—The same as Figs. 226 and 227. Here the characters of the "naevus cells" are well seen: they are polygonal cells with faintly acidophil cytoplasm and round or ovoid nuclei. Amongst them are several large, elongated histiocytes loaded with brown melanin pigment.

Haemalum and Eosin × 450.

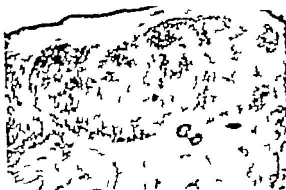


Fig. 229

Naevus Pigmentosus (*Melanoma*).—In this example the epidermis is stretched over the relatively deeply placed tumour, which consists of packed naevus cells and many pigmented cells. The tumour mass is well defined.

Haemalum and Eosin × 15



Fig. 230

Naevus Pigmentosus (*Melanoma*).—*Edge of the same specimen as Fig.* 229.—The closely packed naevus cells and interspersed pigment-bearing cells (melanophores) are shown in more detail. A small blood vessel is seen at the side amongst the tumour cells.

Haemalum and Eosin × 100.



FIG. 231

Naevus Pigmentosus et Pilosus (Melanoma) from chin.—There is an excess of hair follicles with their associated sebaceous glands and some sweat glands. In the dermis between the hairs are small groups of naevus cells.
Haematoxylin and Eosin × 20.

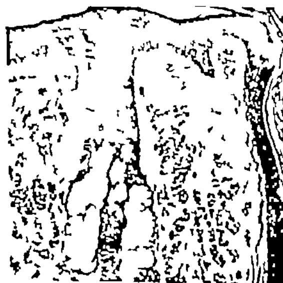


FIG. 232

Naevus Pigmentosus et Pilosus (Melanoma) from chin.—A portion of the same naevus as Fig. 231 to show the groups of naevus cells in the dermis between the hair foll
Haematoxylin and Eosin × 105.

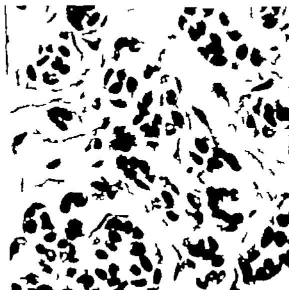


Fig. 233

Naevus Pigmentosus et Pilosus (Melanoma) from chin.—Columns of typical naevus cells from the same specimen as Figs. 231 & 232.

Haemalum and Eosin × 450.



Fig. 234

Naevus Pigmentosus.—Portion of naevus to show naevus cells in groups and masses in the dermis.

Haemalum and Eosin 80



Fig. 235

Naevus Pigmentosus (*Melanoma*).—This example is shown because of the amount and density of the stroma. In this stroma are groups of typical naevus cells, more numerous just under the epidermis—which is stretched over the surface. There are also groups of pigment carrying cells (melanophores) in the superficial part.

Hematoxylin and Eosin × 60.

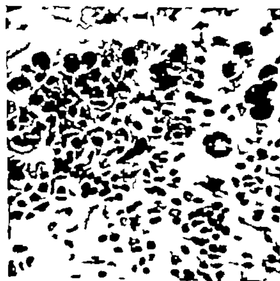


Fig. 236

Naevus Pigmentosus (*Melanoma*).—The same section as in *Fig.* 235, *superficial portion*.—Along the edge of this layer are many pigment-carrying cells (melanophores); the deeper cells are of ordinary naevus type.

Hematoxylin and Eosin × 320.

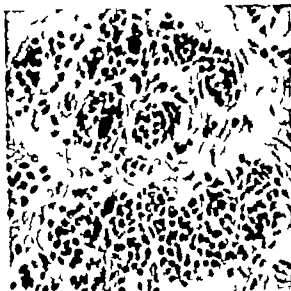


Fig. 237

Naevus Pigmentosus (Melanoma).—The same as Figs. 235 & 236, *deeper portion, to show more naevus cells, fewer melanophores, and greater amount of fibrous stroma.*
Haemalum and Eosin × 320.

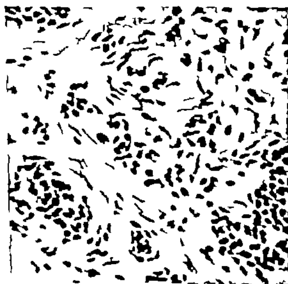


Fig. 238

Naevus Pigmentosus (Melanoma).—The same as Figs. 235, 236 & 237, *deepest portion. Here the fibrous stroma is abundant and many of the naevus cells are becoming isolated by it and are atrophic.*
Haemalum and Eosin × 320



Fig. 239

Blue Naevus.—The term "blue" refers to its clinical appearance. The section shows hyperkeratosis and slight hyperplasia of the epidermis, also some lymphocytic infiltration around the small vessels of the superficial dermis. The chief feature is the presence around the sweat glands of naevus cells and melanophores.

Haemalum and Eosin × 50.



Fig. 240

Blue Naevus. The same as Fig. 239, area of sweat glands.—The position of the pigment containing cells is well seen here.

Haemalum and Eosin × 75.



FIG. 241

Blue Naevus *The same as Figs* 239 & 240 *A portion of sweat gland*.—The cells bearing the melanin pigment lie in the stroma alongside the coil of sweat gland

Haematoxylin and Eosin × 400



Fig. 242

Naevus Pigmentosus (Melanoma).—This tumour illustrates the difficulty in deciding whether or not melanoma (pigmented naevus) is malignant. Parts were regular and benign, other parts had cells irregular in size, shape and arrangement. The portion portrayed shows much hyperkeratosis on the surface and very irregular and acanthotic epidermis. Lying in the situation of the dermal papillae are groups of cells of the ordinary naevus cell type, but mixed with these in places are large irregular cells carrying pigment. Along the lower edge of the epidermis are irregular pigmented cells.
Haemalum and Eosin × 85.

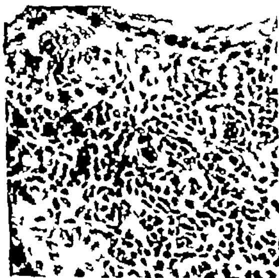


Fig. 243

Naevus Pigmentosus (Melanoma).—*The same as Fig. 242, surface zone.* This illustrates the variety in size, shape and pigment-content of the tumour cells. The epidermis atrophic and stretched over the tumour. *Haemalum and Eosin* 400.

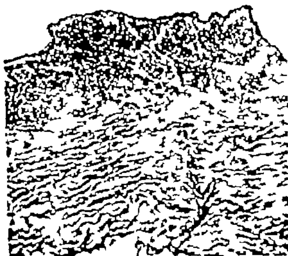


Fig. 244

Malignant Naevus Pigmentosus (Malignant Melanoma).—This tumour arose at one end of linear benign pigmented naevus (Fig. 246) which had been present for many years. This area is malignant. It consists of masses of tumour cells which are invading the epidermis and permeating indefinitely into the dermis.

Haematoxylin and Eosin × 60.

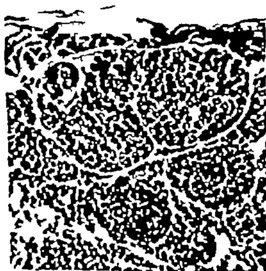


Fig. 245

Malignant Naevus Pigmentosus (Malignant Melanoma).—A portion of the surface of the preceding (Fig. 244) specimen to show the tumour masses invading the epidermis, which is much atrophied. There is no definite evidence of any pigment in this portion.

Haematoxylin and Eosin × 330.



Fig. 246

Naevus Pigmentosus (*Melanoma*) *non-malignant area.*—The specimen was taken from the opposite end of the pigmented part to that from which the malignant tumour (Fig. 244) arose. It merely shows a number of large elongated cells heavily laden with dark brown (melanin) pigment.

Haematoxylin and Eosin × 200



Fig 247

Malignant Naevus Pigmentosus (Malignant Melanoma).—A general view given of the tumour which consists of mass of naevus cells covered by epidermis stretched over the surface It ill defined on its deeper aspect and few areas of pigment are seen

Haematoxylin and Eosin 20

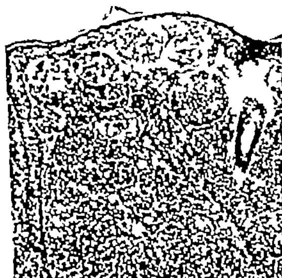


Fig 248

Malignant Naevus Pigmentosus (Malignant Melanoma).—*The same as Fig 247 surface zone of tumour*.—The epidermis on the surface thinned and being encroached upon by irregular groups of large cells of which some show pigment granules A little deeper are number of deeply pigmented cells, and few lymphocytes in the meshes of the cavity stroma Deeper still the tumour cells are more uniform in size, densely packed, and show only few pigmented cells which are indistinguishable from naevus cells

Haematoxylin and Eosin 110



Fig. 249

Malignant Naevus Pigmentosus (Malignant Melanoma).—The same as Figs. 247 & 248 middle zone of tumour.—The tumour cells here are irregularly arranged in masses with scanty stroma in which run delicate blood vessels. The cells themselves are unequal in size and shape and none show pigment.

Hamilton and Ewen ×170



Fig. 250

Malignant Naevus Pigmentosus (Malignant Melanoma).—The same as Figs. 247, 248 & 249, deepest zone.—In this part very few tumour cells are present but many large histiocytes loaded with melanin pigment are seen. The stroma is more abundant and very vascular.

Hamilton and Ewen ×170



FIG. 251

Naevus pilosus.—The main feature of this specimen is the relatively large number of hairs — cut in cross section. The stroma is fibrous and there are no naevus cells.
Haematoxylin and Eosin × 80



FIG. 252

Nevus Pilonidalis (Pilonidal Sinus).—The surface epidermis extends as a lining into the sinus but stops abruptly before the base is reached. Surrounding the whole area of the sinus is a thick zone of dense chronic inflammatory fibrous tissue.

Hamilton and Ewen × 4½



FIG. 253

Nevus Pilonidalis (Pilonidal Sinus).—Middle zone, where the epithelial lining terminates and the sinus beyond is lined by inflammatory fibrous tissue, in which are hair follicles. In the lumen are many small hairs cut at various planes and mixed with epithelial debris.

Hamilton and Ewen × 14



FIG 254

Naevus Pilonidalis (Pilonidal Sinus) part of wall of deeper area — Numerous hairs, mostly of small size, are cut transversely or obliquely and are surrounded by fibrous tissue in which are small blood vessels and many chronic inflammatory cells

Haemalum and Eosin × 85



Fig. 255

Naevus (Epithelioma) Adenoides Cysticum.—There proliferation of hair follicles, from the outer surface of which, and from the basal layer of the epidermis, anastomosing strands of basal cells radiate into the surrounding dermis; cystic spaces are forming in the centre of epithelial masses. The stroma which supports this cellular network is rich in connective tissue cells.

Haemalum and Eosin × 25.



Fig. 256

Naevus (Epithelioma) Adenoides Cysticum.—High power view of Fig. 255.

Haemalum and Eosin × 100



Fig. 257

Naevus Sebaceus.—Low power view showing hyperkeratosis, acanthosis, proliferation of sebaceous glands, cystic dilation of sweat-gland ducts, no cellular reaction and no naevus cells.

Haemalum and Eosin × 10.



Fig. 258

Naevus Sebaceus.—Higher power view of Fig. 257 showing hypertrophy and proliferation of sebaceous glands, and some lymphocytic infiltration. Naevus cells are absent.

Haemalum and Eosin × 25.



FIG. 259

Naevus Sebaceus.—Higher power view of Fig. 257 showing hyperkeratosis, acanthosis, occasional cystic dilatation of sweat-gland ducts, and some dilatation in the coil of the sweat-gland (bottom right)

Haematoxylin and Eosin 25



FIG. 260

Naevus Sebaceus.—The tumour is composed of masses of hyperplastic sebaceous glands situated immediately beneath the epidermis, which is raised up over them.

Haemalum and Eosin × 20



FIG. 261

Naevus Sebaceus. *The same as Fig.* 260.—This shows in more detail the sebaceous glands, one of which is opening on the surface. There is some lymphoid infiltration between the glands and the epidermis but no naevus cells are present.

Haemalum and Eosin × 75



Fig 262

Naevus Sebaceus—Portion of naevus sebaceus showing hyperkeratosis, plugging of sebaceous gland orifice, regular acanthosis, hypertrophy and proliferation of sebaceous glands to the left of the section, cyst formation in sweat-gland ducts, and very slight degree of lymphocytic infiltration There are no malignant changes present in this area

Haemalum and Eosin 20.



Fig 263

Naevus Sebaceus showing malignant change.—Acanthotic epidermis from another portion of the same naevus sebaceus as shown in Fig 262 This section shows small commencing nodule of basal cell carcinoma at the left-hand side of the section.

Haemalum and Eosin 65



Fig. 264

Naevus Sebaceus showing malignant changes.—Acanthotic epidermis from same naevus sebaceus as shown in Figs 262 and 263. A squamous cell carcinoma is developing, and there is an intense surrounding lymphocytic and polymorph infiltration.

Haemalum and Eosin 65



FIG. 265

Naevus Sebocystomatosus, Papilliferous type. Portion of cystic area.—The wall of the cyst is lined by thin layer of cells but in places papillary ingrowths arise from these and project into the cyst. One small papilla is seen attached to the wall and part of larger one lying within the cyst. The wall of the cyst is formed by layers of dense fibrous tissue. *Hematoxylin and Eosin* 13.



FIG. 266

Naevus Sebocystomatosus, Papilliferous type. The small papilla shown in preceding figure (Fig. 265).—The single layer of cells forming the lining of the cyst is seen and it is continued into the papilla which is composed of similar cells closely packed. Amongst these are paler areas which are delicate processes of the supporting stroma carried in with the epithelium as cores to the epithelial groups of cells forming the papilla. T the side the very early formation of another projection, seen as small aggregation of the epithelial cells around portion of stroma. The underlying stroma is formed of dense fibrous tissue. *Hematoxylin and Eosin* 95.



Fig. 267

Naevus Syringadenomatosus.—Cystic dilatations of the sweat gland ducts constitute the lesion. The ducts are more numerous than normal. In this specimen there was no evidence of hyperplasia of the sebaceous glands and no papilliferous process were found projecting into the cysts.

Hamilton and Evans × 40.



Fig. 268

Naevus Syringadenomatosus.—Throughout the middle and lower portion of the dermis there are numerous dilated ducts of sweat-glands.

Hamilton and Evans 100



Fig. 269

Naevus Syringadenomatosus Papilliferus.—Cystic dilatation of varying degree is seen in the sweat-gland ducts superficial to the coil. Ducts are seen to open on to the surface through large cup-shaped aperture. The epithelial cells lining this aperture are similar to those of normal sweat-gland duct, and are continuous at the sides with the epidermis. From the floor of the cup-shaped depression numerous papillary processes project towards the surface. They consist of fibrous tissue stroma covered by sweat-gland duct epithelium. The stroma is packed with plasma cells.

Haxthausen and Evans × 8



Fig. 270

Naevus Syringadenomatosus Papilliferus.—This shows papilliferous processes projecting on to the surface from floor of sweat gland duct epithelium. The epidermis has disappeared. The sweat-gland ducts are tortuous and show varying degree of dilatation. Plasma cells are numerous in the stroma of the processes.

Haxthausen and Evans 22

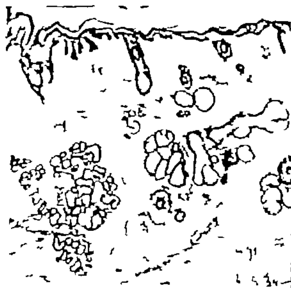


Fig 271

Naevus Syringadenomatosus Papilliferus.—Low power of field adjacent to that shown in Fig 270, at the edge of the tumour The epidermis is intact here, there is tortuosity and dilatation of the sweat-gland ducts The sebaceous glands are normal. There are areas showing compact infiltration of plasma cells.

Haemalum and Eosin × 22.



Fig 272

Naevus Syringadenomatosus Papilliferus.—A higher power view of Fig 271 to show normal coil-epithelium and cystic dilatation of the more superficial ducts.

Haemalum and Eosin × 80.



Fig. 273

Naevus Syringadenomatosus Papilliferus.—A cystic dilatation of a sweat gland duct opening on to the surface. The adjacent epidermis is continuous with the wall of the cyst. Papilliform processes project into the interior of the cystic opening.

Hamilton and Evans × 30.



Fig. 274

Naevus Syringadenomatosus Papilliferus.—Surface cystic dilatation similar to that shown in Fig. 270. The papilliferous projections are covered with sweat-gland duct epithelium, and the stroma contains numerous plasma cells.

Hamilton and Evans × 50.

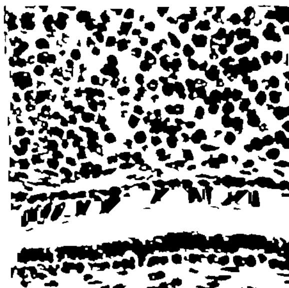


FIG. 275

Naevus Syringadenomatosus Papilliferus.—This section shows from above downwards, the stroma of a papilliferous process packed with plasma cells, the lining epithelium of a sweat gland duct forming a covering for the process, the lumen of the cavity and its covering of [illegible] epithelium and some plasma cells in the adjacent dermis.

[illegible] and [illegible] 450



Fig. 276

Naevus fibromatosus.—This pedunculated papilloma consisting of matrix of loose connective tissue in which are thin-walled blood vessels and covering which is layer of epidermis showing reticular acanthotic arrangement and some hyperkeratosis. The stalk is covered with stretched epidermis.

Haematoxylin and Eosin 14

LYMPHANGIOMA (Fig. 277) is composed of dilated lymph spaces of varying size and shape. These cavernous spaces may occur at any depth in the dermis, but when situated immediately beneath the epidermis they have a clinical appearance of small tense bullae resembling frog spawn, to which the term *lymphangioma circumscriptum* (Fig. 278) is applied.

The HAEMANGIOMA is a much more cellular tumour than the lymphangioma, and three distinct varieties occur

The *capillary angioma* (Figs. 279-284) consists of packed masses of angioblastic cells and capillaries formed by them, situated in the upper dermis.

The *cavernous angioma* (Fig 285) occupies a deeper situation in the dermis and in addition to angioblastic cells and aberrant capillaries, large irregularly shaped thin-walled blood spaces are present.

Angioma serpiginosum (Figs. 286 and 287).—This is merely a variant of the capillary angioma. It extends irregularly throughout the dermis and even more deeply the strands of vaso-formative cells and vessels may be considerably separated in places by collagen fibres. Oedema and infiltration by inflammatory cells may be superadded but are not essential features of the condition.

ANGIOKERATOMA (Figs. 288 and 289) This condition occurs on the fingers, toes, knees, elbows, and scrotum and generally establishes itself at an early age. In a typical case there is also a history of acrocyanosis or erythema pernio.

The histological picture shows marked hyperkeratosis, acanthosis and hypertrophy of the rete pegs, so that the rete on section is in the form of a network. In the papillae and superficial part of the dermis, there are dilated blood vessels and lacunae containing blood, a varying amount of polymorph infiltration, and some fragmentation and disintegration of collagen fibres and elastic tissue.

GLOMUS TUMOUR (Figs. 290-292). This is a specialised form of vascular growth which has the characters of the normal glomus—a mechanism for regulating the blood supply in certain parts of the body especially the fingers and toes. The tumour consists of vascular channels with an endothelial lining, immediately outside of which are several layers of polygonal cells (the "glomus cells") Around some of the vessels there is a supporting collagenous framework which contains plain muscle cells and abundant nerve fibres, mainly of the non-myelinated type. The nature of the glomus cell is debateable, it is regarded by some as an angioblast, even capable of forming elastic fibrils, by others it is

considered to be a myoblast. Because of the rich nerve supply these tumours are usually painful.

ADENOMA SEBACEUM (Figs 293 and 294). This tumour occurs as a small red nodule varying in size from a pin head to a pea. It is situated on the face, is always multiple, and is found in mental defectives

The title adenoma sebaceum is a misnomer for the histological appearance is that of an angioma. The sebaceous glands are certainly large and moderately numerous, but this is only to be expected in the skin of the nose and cheeks, and in association with a liberal vascular supply

The epidermis is stretched and thinned and the dermis contains numerous blood spaces and capillaries in varying degrees of dilatation. The supporting connective tissue is more cellular than normal, and the sebaceous glands are large but show no pathological changes and are not abnormally numerous The lesions, unlike those of naevus sebaceus, do not tend to become malignant.

Malignant vascular tumours—Angioendotheliomata—of the skin are rare They are rapidly growing tumours composed of primitive vessels and angioblastic cells infiltrating into the surrounding tissues. The KAPOSI TUMOUR (Figs 295 298), may be regarded as of this nature In it there is a formation of many irregular vascular spaces and channels, which frequently rupture and give rise to haemorrhages Between these there are many undifferentiated mesoblastic and inflammatory cells The tumour tends to infiltrate both the epidermis and the deeper tissues and it may regress and recur

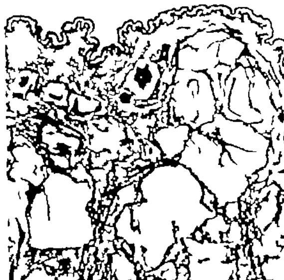


FIG. 277

Lymphangioma.—This tumour consists of large, thin walled cavernous lymph spaces filled with coagulated lymph. These spaces extend from just under the epidermis through the whole thickness of the dermis. The epidermis has been pushed upwards by the mass of spaces. The supporting connective tissue is stained blue.

Haematoxylin Azan Stain × 75



FIG. 278

Lymphangioma (circumscriptum type).—This form of lymphangioma also consists of large cavernous spaces lined by flattened endothelial cells—not always discernible—and delicate reticular supporting tissue. The lymph content has been fixed in situ in several spaces. This type of lymphangioma is always situated superficially in the papillary area of the dermis and the spaces abut on the epidermis.

Haematoxylin and Eosin × 55



Fig. 279

Capillary haemangioma ("vascular naevus"—strawberry type).—This shows the whole extent of the tumour which stretches from the base of the epidermis through the dermis and into the subcutaneous tissue. Hair follicles are seen to be surrounded by it, and in the subcutaneous area, fat spaces and also a few large normal blood vessels are seen in its substance.

Haematoxylin and Eosin × 6



Fig. 280

Capillary haemangioma ("vascular naevus"—strawberry type).—A higher power view of its superficial portion. The tumour tissue consists of closely packed capillary vessels, with a few larger blood spaces, and extends practically to the epidermis, occupying the dermal papillae. Part of a hair follicle is seen at the bottom right.

Haematoxylin and Eosin × 55.



FIG. 281

Capillary haemangioma ("vascular naevus"—strawberry type).—High power view of the deeper portion. Part of the subcutaneous fat is seen with tumour abutting on it. The tumour here is composed of closely packed endothelial cells amongst which only a few minute capillary lumens have developed.

Hamilton and Ewen × 145.

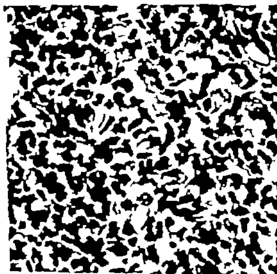


FIG. 282

Capillary haemangioma ("vascular naevus"—strawberry type).—High power view of the preceding showing the endothelial type of cell and a few developed capillaries.

Hamilton and Ewen × 475.



Fig. 283

Capillary haemangioma ("vascular naevus") showing [illegible] disposition in the dermis similar to those of Fig. 279, but having larger blood spaces.

Haematoxylin and Eosin × 14.



Fig. 284

Capillary haemangioma ("vascular naevus")—A higher power view of the surface. There is the same endothelial vaso-formative tissue as seen in Fig. 280 but in this case it is developing into larger blood spaces, almost approaching the cavernous type.

Haematoxylin and Eosin × 75.



Fig. 285

Cavernous *haemangioma*.—Note that the blood spaces are large and thin-walled. There are also more solid parts with small capillary-type vessels and endothelial cells.
Haematoxylin and Eosin × 20.



Fig. 286

Angioma serpiginosum.—The variant of the haemangioma. It has the same vaso-formative cells and blood spaces formed from these which vary in size from capillary to venule. The tumour is ill-defined, being irregularly distributed in the cutaneous and subcutaneous areas.

Hamilton and Evans × 110.

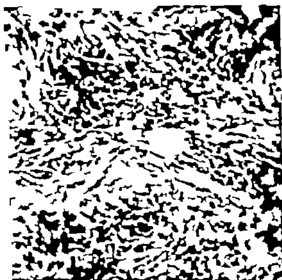


Fig. 287

Angioma serpiginosum.—T shows in more detail number of small capillary spaces and their attendant cells. These are embedded in fibrous stroma.

Hamilton and Evans 210



FIG. 288

Angiokeratoma.—This shows hyperkeratosis, acanthosis and papillary hypertrophy; blood spaces and dilated vessels; some perivascular leucocytic infiltration; fragmentation of collagen fibres in the middle dermis.

Haematoxylin and Eosin ×60.



FIG. 289

Angiokeratoma.—The features are similar to those shown in Fig. 288. Note that the lacunae which are situated within the area of the epidermis are actually bounded by wall of fibrous tissue.

Haematoxylin and Eosin ×30.



Fig. 290

Glomus tumour.—This consists of cavernous blood spaces, the walls of which are thicker than those of the preceding hæmangiomas.

Hæmalum and Eosin × 20.



Fig. 291

Glomus tumour.—Higher power showing the edge of a large blood space and several small spaces. The spaces have an internal lining of endothelium surrounding which is a mantle of several layers of glomus cells. The nature and function of these cells are the subject of conjecture. They have been regarded as being of endothelial origin and also as primitive plain muscle cells (myoblasts). Nerve fibrils—not stained in this preparation—are usually numerous around the vascular spaces.

Hæmalum and Eosin × 110.

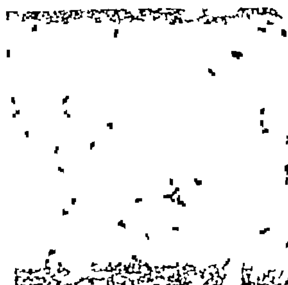


FIG. 292

Glomus tumour.—This example shows the greater part of the tumour to be composed of the glomus cells. Amongst these are blood spaces, many small, few large. There is delicate reticular stroma between the groups of cells.

Picro-Mallory × 100

Fig. 293

Adenoma Sebaceum.—This shows hyperplasia of the sebaceous glands, and dilated blood spaces.
Haematoxylin and Eosin × 15.

Fig. 294

Adenoma Sebaceum.—A high power view of Fig. 293 to show numerous blood spaces of varying sizes. The tumour is a combination of angiomatous tissue and glandular hyperplasia.
Haematoxylin and Eosin × 70.



Fig. 295

Kaposi Sarcoma—A form of Angio-endothelioma; skin area. The epidermis is stretched and thin with slight hyperkeratosis. The tumour occupies the dermis and extends deeply to the underlying tissues. This view shows the numerous small vessels with surrounding supporting cells and haemorrhage into the stroma.

Haemalum and Eosin × 75.



Fig. 296

Kaposi Sarcoma—The same case as Fig. 295; subcutaneous area. The fatty tissue is infiltrated in the same fashion as the skin.

Haemalum and Eosin × 75.



Fig. 297

Kaposi Sarcoma.—The same case as Figs. 295 & 296 showing the invasion of muscle by the tumour

Hæmalum and Eosin × 75.



Fig. 298

Kaposi Sarcoma.—*The same case as Figs.* 295, 296 & 297. A detailed view in which can be seen several small vessels accompanied by spindle-shaped fibroblastic cells cut in various planes

Hæmalum and Eosin × 275

Cutaneous cysts can be placed in the following categories:—

CONGENITAL

NAEVUS SYRINGADENOMATOSUS
NAEVUS SYRINGOADENOMATOSUS PAPILLIFERUS.
NAEVUS SEBOCYSTOMATOSUS
EPITHELIOMA (NAEVUS) ADENOIDES CYSTICUM.
PILONIDAL CYST

ACQUIRED

SEBACEOUS RETENTION CYST (Figs. 299-302)
MILIUM (Figs. 303-305).
IMPLANTATION CYST (Figs. 306-308).
MUCOUS (OR MYXOMATOUS) CYST (Figs. 309 and 310)
CYSTIC BASAL-CELL CARCINOMA (Figs. 344-346).

The congenital cystic tumours fall into the category of *naevus* and are described in that general section, while the cystic variety of basal-cell carcinoma is illustrated and described in the section on carcinoma.

Of the acquired cysts, the sebaceous cyst and milium are of common occurrence, the implantation cyst is not infrequently seen, but the mucous cyst is of extreme rarity. The sebaceous retention cyst is caused by prolonged blockage of a sebaceous gland orifice by a comedo, or by a superficial infective process producing complete stenosis of the duct. The result is a dilatation of the gland with atrophy of all but the periphery of the lobules, and the formation of a sac filled with keratin and sebaceous material. The wall of the cyst is composed of a number of epithelial cells arranged in layers resembling a stretched portion of epidermis. The contents of the cyst may become calcified.

Milium occurs on the forehead, the temples, the eyelids and the malar regions and cheeks. The lesions may be single or multiple and are sometimes numerous. The cyst is small and is situated immediately under the epidermis, being separated from it only by a narrow strip of dermis. The cyst wall is formed by two or three layers of flattened epidermal cells and the contents are strands of keratin material. These small cysts often extrude themselves from the skin spontaneously, the pressure which they exert causing an atrophy of the overlying structures. No reliable evidence is available to indicate their mode of origin, but it is presumed that they are derived from lanugo hair follicles, or perhaps from sweat-gland ducts.

The implantation cyst is produced by the mechanical intrusion of a portion of the epidermis into the dermis as a result of trauma. The

wall is formed by epithelial cells arranged in layers corresponding to those of the epidermis, and direct continuity between the epidermis and the wall of the cyst may be traced in some cases The contents of the cyst are keratin strands.

The mucous cyst occurs in the region of the finger nails, usually on the dorsum of the terminal phalanx or on the side of a finger It is produced by a mucinous degeneration of collagen fibres in a localised area of the dermis. There is no epithelial lining to the cyst the wall of which is formed by collagen fibres In places the fibres immediately surrounding the cystic space are thin and form an open lace work in which mucin can be demonstrated but the major portion of the wall of the cyst is composed of collagen fibres which are normal in appearance The mucous cyst is difficult to eradicate, and recurrence may take place even after the apparent complete excision of the affected area.

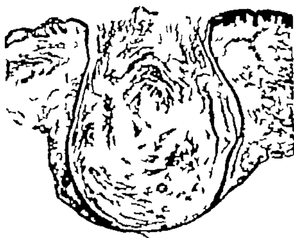


Fig. 299

Sebaceous Retention Cyst.—The entire sebaceous gland filled with keratin and sebaceous material; its glandular structure is lost and reduced to sac, the wall of which consists of few flattened epithelial cells. The ostium of the follicle is greatly dilated, and the epithelial wall of the cyst is continuous with the epidermis.

Haemalum and Eosin × 20.

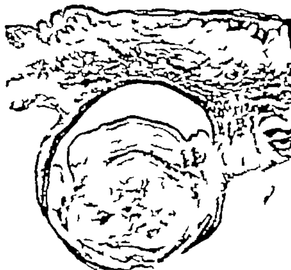


Fig. 300

Sebaceous Retention Cyst.—This section is on different plane from that in Fig. 299 and shows the keratin-containing sac completely shut off from the surface.

Haemalum and Eosin × 20



Fig. 501.

Sebaceous Cyst.—The glandular structure of the sebaceous gland has disappeared, and the gland has become transformed into an epithelial-lined sac containing keratin.
Haematoxylin and Eosin ×23.

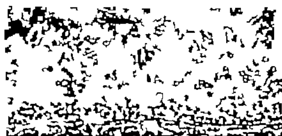


Fig. 502.

Wall of Sebaceous Cyst.—In the upper portion is seen the keratinised contents of the cyst. Immediately beneath this thin layer of epidermal epithelium bounded by the fibrous tissue of the dermis.
Haematoxylin and Eosin ×140.

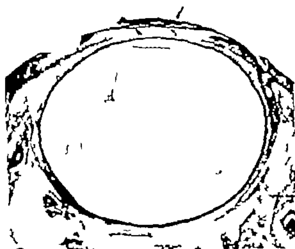


Fig. 303

Milium.—The cyst situated in the superficial portion of the dermis, and separated from the stretched epidermis by thin band of dermis. Serial sections give no indication of the tissue from which the cyst has been derived, nor does it open on surface.

Haematox. and Eosin × 25

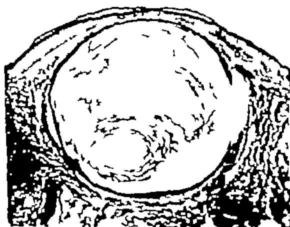


Fig. 304

Milium.—The contents of the cyst are composed of strands of keratin.

Haematox. Azan Stain 25

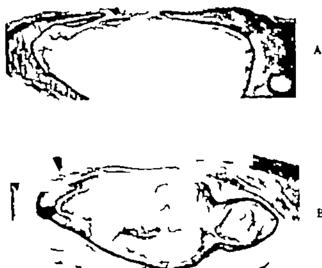


Fig. 306

Implantation Cyst.—A—Shows the point at which the epidermis became invaginated to form the cyst, there being continuity of the cyst wall and the overlying epidermis B—The cyst cut in different plane so that it appears unconnected with the surface The wall of the cyst is formed by thin layer of flattened epidermal cells which are undergoing extreme cornification and the contents of the cyst is quantity of shed cornified material

Hamilton and Evans 10



Fig. 307

Implantation Cyst.—The contents are strands of keratinised material.

Haematoxylin and Eosin ×18.



Fig. 308

Implantation Cyst.—The wall is several cells thick, and is identical with modified and compressed epidermal structure. Stratum granulosum cells are present and fully developed keratin has been produced.

Haematoxylin and Eosin ×400.

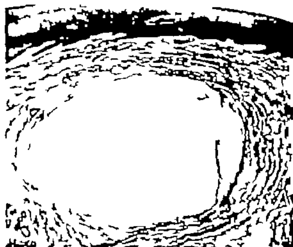


FIG. 309

Mucous Cyst.—There is no cellular lining to the cyst, which occurs as cavity in the dermis resulting from mucoid degeneration of collagen.

Haemalum and Eosin × 30.



FIG. 310

Wall of Mucous Cyst.—This composed of dense collagen fibres hich in some places are rarefied to form fine open network showing traces of mucin.

Haemalum and Eosin × 110.

Tumour formation may develop in any of the epidermal structures or the component parts of the dermis, so that both benign and malignant growths which are commonly seen in other tissues may also be met with in the skin. Tumours such as molluscum contagiosum, the contagious verrucae, and certain of the naevi are peculiar to the skin alone.

THE FIBROMA (Figs. 311 and 312) is to be distinguished from an ordinary nodule of scar tissue, or a bunion due to irritation and pressure, by the whorled arrangement of the fibrous strands composing it. It is usually well defined and dense, and numerous fibroblasts may be present or it may be composed almost entirely of collagen fibres, depending on its age and rate of growth. The cellular form may recur on removal and ultimately develop definite malignancy as a fibro-sarcoma.

MOLLUSCUM FIBROSUM (Fig 313) is a multiple form of fibroma. The nodules may be pedunculated and the matrix oedematous or even myxomatous. While the tumours are usually distributed along cutaneous nerves there are frequently no nerve elements demonstrable in the superficial nodules.

FIBROUS EPULIS (Fig. 314) is yet another variety of fibroma, found along the gum or tooth margin.

CHONDROMA (Figs. 315 and 316). This is an unusual form of cutaneous growth, but it may form as a "callosity" e.g. over the knuckles of the fingers It has the usual characters seen in chondromata in other situations—hyaline cartilage bounded by fibrous tissue.

MYOMA (Figs. 317 and 318), of the plain muscle variety—Leiomyoma—occurs in the dermis. It is a rare tumour and the usual site is the face It is small in size and is composed of whorls of plain muscle fibres.

XANTHELASMA, XANTHOMA (Figs. 319-322) AND XANTHOMA TUBEROSUM MULTIPLEX (Figs 323 325) must be considered as doubtful tumours from the pathological standpoint, although clinically they can be placed in the tumour group. In all three varieties there is a localised hyperplasia of histiocytes in the upper and middle dermis. These cells appear large, clear and vacuolated (foamy-cells) in ordinary paraffin sections, but in frozen sections appropriately stained they are seen to be laden with fat or lipoid In xanthoma tuberosum numerous large multinucleated histiocytes (Touton's giant-cells) are also present.

A local intra-cellular or a general metabolic upset in lipoid metabolism is the immediate cause, and xanthoma and xanthoma tuberosum occur in association with diabetes (compare with necrobiosis lipoidica) Xanthelasma is found on the eyelids in otherwise healthy individuals of all ages.

In all three types of xanthoma the cells involved belong to the reticulo-endothelial system and the hyperplasia is of a type which permits of their inclusion along with the reticuloses.

THE CONTAGIOUS VERRUCAE (Figs. 326-336).

This group of contagious cutaneous papillomas comprises several well defined varieties, each of which is a modification of a uniform type of epidermal and dermal hypertrophy The various representatives of the group have the following clinical titles — Verruca Plana Verruca Vulgaris, with its subdivisions, Filiformis, Digitata, Plantaris, and Condyloma Acuminatum.

In verruca plana the hyperplasia is limited to the epidermis. This tissue is uniformly thickened and shows a hyperkeratotic stratum corneum in which parakeratotic cells may occur in small groups, an increase in the thickness of the stratum granulosum which varies directly with the thickness of the overlying horny layer and marked acanthosis which may have the appearance on section of a thick meshed network in its deeper part owing to inclusion of the papillae The basal layer is regular and normal in appearance.

In verruca vulgaris there is a similar hyperplasia of the epidermis, but a special feature is the elongation of the rete pegs, which project downwards as finger like processes showing a tendency to curve inwards towards the central axis of the lesion There is a corresponding elongation of the papillary processes. The stratum corneum is greatly thickened and in it are to be found layers of parakeratotic cells. The cells of the basal layer are normal, and the dermo-epidermal junction is regular in outline. Sweat-gland ducts may traverse the lesion and in some cases there is a mild degree of inflammatory reaction. In the digitate and filiform varieties the hyperplastic formation projects upwards from the surface of the skin as a group of narrow finger-like processes, while in the verruca plantaris the whole lesion is compressed into the substance of the dermis and is surrounded by a callosity In the condyloma acuminatum the whole process has a more solid and succulent appearance than in the other varieties

Degeneration of the rete cells may be seen in all varieties of verrucae and it bears no relation to the age of the lesion. It takes the form *of vacuolation of the cell and the development of eosinophil droplets*, which may be kerato-hyalin in the cell cytoplasm The nucleus is pyknotic and pushed to one side, the cell membrane is thickened and the prickles are lost. This process may affect single cells or groups of cells, it occurs at any point in the rete above the basal layer and the degenerated cells eventually appear in the stratum corneum. The degenerative change reaches its most extreme degree in the apparent complete liquefaction of the cell which is transformed into an eosinophil staining anuclear mass A number of adjacent cells may undergo this complete dissolution, and partially degenerated cells may be found

embedded in such a homogeneous mass. Cellular degeneration is seen most constantly and in its most advanced stages, in the verruca plantaris That it is a process peculiar to the verrucous tissue and not dependent merely on pressure or to the heaping up of stratum corneum is shown by the fact that it does not affect the epidermis which forms the callosity surrounding the verruca, the rete and stratum corneum of this surrounding hypertrophied epidermis being sharply demarcated from the adjacent degenerated rete and stratum corneum of the verruca (Fig. 333). The degenerative change may ultimately involve the entire verruca with the result that it separates and is extruded (Fig. 334), thus bringing about a spontaneous cure of the condition.

The verrucae are differentiated from the senile keratoma by the degree of acanthosis and the regularity of the basal layer which they present, and by the constant presence of an inflammatory reaction at the base of the keratoma.

In the senile or seborrhoeic wart (Figs. 220 and 221) the acanthosis invariably presents the appearance of a network on section, horny plugs project downwards from the surface into the epidermis, and the lesion has a flat appearance, features which serve to distinguish it from the contagious verrucae. In the condyloma acuminatum there is a verrucous epidermal hyperplasia which is absent in the condyloma latum (Fig 182) and in the latter there is the dense plasma cell infiltration common to all syphilitic lesions.

Molluscum Contagiosum (Figs. 337 339).

This lesion consists of an epidermal hyperplasia which is caused by the action of a filterable virus on the cells of the rete. A small tumour varying in size from a pinhead to a pea is produced in this way

The hyperplasia of the epidermis is considerable and it projects into the dermis forming a mass with a lobulated outline. At the same time it protrudes above the level of the skin surface and carries a covering of the surrounding stretched epidermis with it. The junction between the basal layer of the epidermal mass and the dermis is regular and the cells of the basal layer appear normal. In the lower strata of the prickle celled layer eosinophilic inclusion bodies appear in individual cells and as the superficial central portion is approached an increasing number of cells contain these bodies. The stratum granulosum is thickened and the cells containing the inclusion bodies pass through it and form a dense mass superficial to it, where they are surrounded by a small amount of keratin. These eosinophilic inclusion bodies are pear shaped, and their narrow pole is more translucent than the rest of the body giving the appearance of a vacuole. They lie in a cavity in the cell protoplasm, and the cell nucleus is pushed to one side. By appropriate methods they can be removed from the containing cell and shown to consist of an envelope which encloses numerous elementary bodies.

Basal-cell Carcinoma (Figs. 340-346) This tumour is of slow growth and is only locally malignant. It is composed of masses of small, round or polygonal deeply staining epithelial cells of basal-cell type. The cells which bound the masses at their periphery may be more columnar and as a result of compression all the cells may become spindle-shaped. Degeneration and liquefaction of groups of cells may produce cystic spaces of varying size within the tumour masses

The invading cells penetrate the dermis for varying depths, and in old-standing tumours they may reach the subcutaneous tissue, muscle cartilage, and bone. The masses may take the form of solid columns or of thin strands which form a network. The point of origin may be either the epidermis itself or the epithelium of the hair follicles, sebaceous glands, sweat-glands, and sweat ducts A tumour formation which arises from the epidermal appendages has no continuity with the epidermis itself The cell masses, whatever their point of origin, are always clearly demarcated from the surrounding dermis which shows a variable degree of fibroblastic reaction and an infiltration with lymphocytes. Superficial ulceration of the central portion takes place sooner or later

In a proportion of basal-cell carcinomas there is an admixture of tumour growth of squamous-cell type (Figs, 363 and 364) and such mixed forms are to be regarded as squamous-cell tumours from the point of view of malignancy

Squamous-cell Carcinoma (Epithelioma) (Figs 347-362). This form of epidermal carcinoma grows rapidly is both locally destructive, and gives rise to metastases. The epithielial down-growths take the form of groups and masses of cells of a type resembling those of the rete mucosum, with or without prickles In the slower growing varieties the tumour cells tend to become differentiated in the same way as those of the rete mucosum with the resultant formation of cornified areas ("pearls" or cell-nests ") In the rapidly penetrating anaplastic forms the tumour cells tend to be elongated or spindle shaped and they show no tendency to cell-nest formation The tumour almost always originates from the epidermis rather than from its appendages, and the infiltrating cell masses are vague in outline and show no clearly defined margin as is the case in the basal-cell variety Around all forms at the growing margin there is an inflammatory reaction ranging from slight to dense leucocytic and lymphocytic infiltration, and the formation of fibroblastic and fibrous tissue

Chronic slow growing varieties do sometimes occur and in them the invading processes are often blunted and seem as if their growth had been arrested by the reaction in the surrounding tissues Degeneration may occur in the cells in the centre of the processes and this may be followed by the deposition of calcium (Fig. 358)

A tendency to extreme cornification is a feature of squamous-cell carcinomas which develop on skin which has been subjected to long

continued irritation from paraffin and X-rays. The development of carcinoma in Lupus vulgaris is almost invariably due to the large and repeated doses of X-rays to which cases of this disease were subjected in the past.

A frequent precursor to squamous-cell carcinoma is a small localised area of hyperkeratosis, which reaches its most extreme degree in the CUTANEOUS HORN (Fig 365)

PAGET'S DISEASE, OR INTRA EPIDERMAL CARCINOMA (Fig. 366). This condition is restricted to the skin of the breast, particularly that of the nipple, and is regarded as an invasion and permeation of the epidermis by tumour cells derived from the lacteal ducts. The malignant cells arising therein grow along the ducts and on reaching the epidermis they permeate its substance. Here they appear as groups of large clear cells lying in lacunae amongst the epidermal cells and producing a thickening of the epidermis while at the same time destroying its solid coherent structure, interfering with the normal process of keratinisation, and leading to parakeratosis and superficial ulceration.

Another malignant condition which shows a clinical resemblance to Paget's disease, but which differs from it histologically is PSORIASIFORM CARCINOMA (Figs 367 370). This variant of cutaneous carcinoma is characterised clinically by its resemblance to a plaque of psoriasis, by the slow peripheral extension of its thread-like edge, and by the tendency to atrophy and spontaneous cure of the older central areas. It may remain superficial throughout its course, showing no tendency to deep penetration but in a proportion of cases this does ultimately occur The term includes Queyrat's erythroplasia and Bowen's pre-cancerous dermatosis. Histologically at the edge of the lesion, there is a basal-cell type of overgrowth which encroaches on the papillary layer of the dermis, and invades the epidermis. In the more central areas the rete pegs are lost, the basal-cell overgrowth has disappeared, and there is fibrosis and some lymphocytic infiltration in the papillary layer

Such plaques are frequently multiple, and it sometimes happens that one of the lesions, or a portion of a large plaque, may assume a much higher degree of malignancy than the remainder This may take the form of a more rapidly growing type of basal-cell tumour or the character of the growth may change to that of a squamous-cell carcinoma



FIG. 311

Fibroma.—The tumour is sharply defined from the surrounding dermis which it compresses to form a capsule around it, and it is covered closely by the epidermis which is stretched over it and shows hyperkeratosis. The tumour is compact, the fibrous tissue staining uniformly pink.

Iron Haematoxylin and Van Gieson × 15



FIG. 312

Fibroma.—Higher power to show the characters of the tumour. It is composed of whorled strands of collagen (stained blue) running in many planes. In the centres of some whorls there are small, well formed blood vessels. There are few fibroblasts in this specimen.

Heidenhain Azan Stain × 70



Fig. 313

Molluscum fibrosum.—One of the many superficial nodules. The epidermis is thinned and stretched over the underlying nodule. This consists of cellular fibrous tissue fairly well defined from the deeper dermis and showing a number of small vessels. No nerve fibres are present.

Haematoxylin and Eosin. ×60



Fig. 314

Fibrous epulis.—This shows the same features as a fibroma.

Iron Haematoxylin and Van Gieson. ×75



FIG. 315

Fibro-chondroma, from the back of the proximal interphalangeal part of finger—This an unusual form of tumour. The section shows it to have dense fibrous periphery and more homogeneous cartilaginous centre. There is hyperkeratosis on the surface. The tumour may have begun as fibrous growth and undergone metaplasia to cartilage in the central part. There is no obvious capsule to be seen.

Hæmalum and Eosin 20

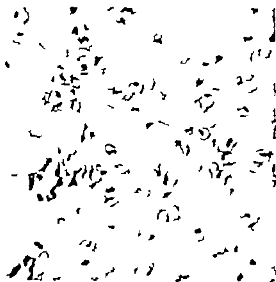


FIG. 316

The same.—High power to show the homogeneous matrix and cells of the cartilage type.

Hæmalum and Eosin 250



Fig. 317

Leio-myoma.—The tumour is composed of bundles of muscle fibres and its position and general outline are evident. It lies in the dermis, slightly separated from the epidermis which is stretched over it, and in its deeper aspect, the muscle bundles are interspersed by fibrous strands.

Haematoxylin and Eosin × 15



Fig. 318

Leio-myoma.—A higher magnification of Fig. 317 to show the bundles of plain muscle interspersed by pink-stained strands of fibrous tissue.

Iron Haematoxylin and Van Gieson × 50.

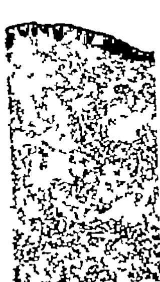


FIG. 319



FIG. 320

FIG. 319. *Xanthoma.*—A portion of the nodule to show the surface epidermis, and the dermis extensively occupied by large, pale-staining cells.
Hematoxylin and Eosin × 75.

FIG. 320. *Xanthoma.*—This is the view given by staining a frozen section for fat—which is still present in the tumor and takes on the yellow dye.
Sudan III and Hematoxylin × 30.

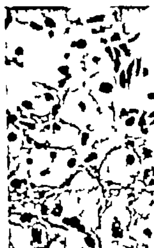


FIG. 321



FIG. 322

FIG. 321. *Xanthoma.*—A detail view of the preceding (Fig. 319), illustrating the vacuolated cytoplasm of the large cells of the nodule.
Hematoxylin and Eosin × 350.

FIG. 322. *Xanthoma.*—The same as Figs. 319–321, but better displayed by the staining method employed.
Heidenhain Azan Stain × 350.

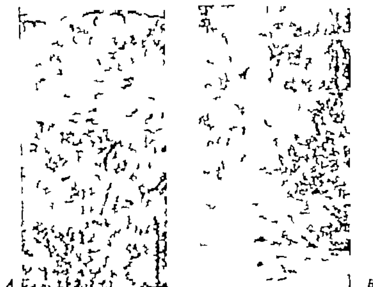


Fig. 323

Xanthoma Tuberosum.—A.—This is the superficial half of the tumour nodule and on its surface is the stretched epidermis. The nodule consists of a great collection of cells of histiocytic type infiltrating the dermis; amongst them are a number of giant cells. B—Deeper half of the nodule. The same picture is presented as in A, but the deep margin is clear cut and bounded by fibrous tissue of the dermis.
Haematoxylin and Eosin × 15.

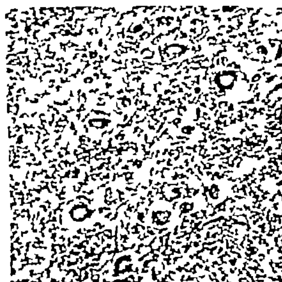


Fig. 324

Xanthoma Tuberosum.—The same as Fig. 323 to show large giant cells (Touton giant-cells) lying amongst the pale, lipoid-containing histiocytes of the nodule.
Haematoxylin and Eosin × 110.

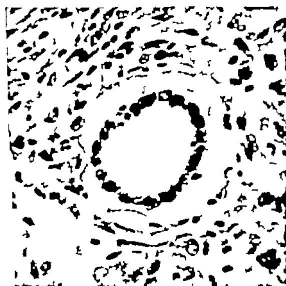


Fig. 325

Xanthoma Tuberosum, same as *Figs* 323 & 324.—A giant cell (*Touton giant-cell*) with zone of vacuolated appearance due to lipoid dissolved out in the preparation of the section. The surrounding cells have slightly vacuolated appearance from the same cause.

Hernandez and Eaton 450



Fig. 326

Verruca Plana.—The section shows acanthosis, and hyperkeratosis.
Haematoxylin and Eosin × 25.



Fig. 327

Verruca Plana.—There hyperkeratosis and some parakeratosis. The rete is and the stratum granulosum shows an uneven hyperplasia. A clump of is present in the region of the stratum granulosum, and below it.
Haematoxylin and Eosin 65.



Fig. 328

Verruca Vulgaris showing hypertrophy of all the layers of the epidermis, complete absence of degenerative changes in the cells of the rete, finger-like processes projecting downwards from the rete and curving inwards towards the central axis of the lesion. There [illegible] an absence of any inflammatory reaction.

Haemalum and Eosin × 18.



Fig. 329

Verruca Vulgaris.—This [illegible] lesion of long standing [illegible]hich has taken the form of cauliflower surface excrescence.

Haemalum and Eosin [illegible] 8.



Fig. 331

Verruca Plantaris.—This lesion shows all the features of verruca vulgaris, modified owing to constant external pressure. A most marked degree of eosinophilic degeneration is seen in many of the rete cells.

Hæmalum and Eosin × 12.

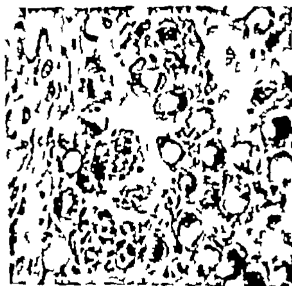


Fig. 33[illegible]

Verruca Plantaris.—This shows clumps of degenerating cells embedded in a homogeneous structure formed by the complete dissolution of surrounding cells. The degenerating cells contain large vacuoles and eosinophil droplets. The cell membrane is thickened, and the prickles have disappeared.

Hæmalum and Eosin × 475.



Fig. 333.

Verruca Plantaris and surrounding callosity.—The structure of the surrounding callosity is that of regular and orderly hypertrophy of all the epidermal layers, and no degenerative process is evident. It is clearly and sharply demarcated from the verruca structure which has undergone gross cellular degeneration, evident both in its rete and stratum corneum.

Hamilton and Earle. × 45.



Fig. 334.

Verruca Plantaris.—The cells of this lesion have undergone complete transformation into homogeneous eosinophil staining areas, as result of which spontaneous cure has been brought about.

Hamilton and Earle. × 55.



Fig. 335

Condyloma Acuminatum.—This lesion from the labium shows the usual changes of verruca vulgaris. Cellular degeneration [is] present, and in the dermis there is no inflammatory reaction, but some vascular dilation. The lesion has [a] more succulent appearance than that seen in verrucae situated on less moist areas.

Hamilton and Eaton 20



Fig. 336

Condyloma Acuminatum.—There are areas of parakeratosis, and degenerated rete cells are included in the hypertrophied stratum corneum. Groups of rete cells are vacuolated and contain eosinophil droplets.

Hamilton and Eaton 75



FIG. 337

Molluscum Contagiosum.—A general view of a small tumour showing the lobulated mass of hyperplastic epidermis protruding into the dermis, and producing a tumour which projects above the level of the surrounding skin surface, carrying a covering of normal epidermis with it. Inclusion bodies are seen in increasing numbers from the lower rete to the central superficial area overlying the stratum granulosum.

Hamilton and Ensor × 20



FIG. 338

Molluscum Contagiosum.—The eosinophilic inclusion bodies are first seen in small numbers in the lower portion of the rete. They become increasingly numerous as the stratum granulosum is approached, and the central depression on the surface of the lesion is filled with keratinised cells containing inclusion bodies.

Hamilton and Ensor × 70

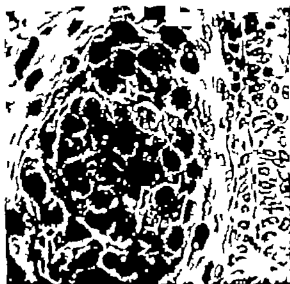


FIG. 339

Molluscum Contagiosum.—The eosinophilic inclusion bodies are pyriform or oval in shape, and many of them appear to contain small vacuoles at their narrow end. This is actually an area where the containing membrane is thinner than over the rest of the body. The nucleus of the epithelial cell is pressed to one side.

Haematoxylin and Eosin. ×400.



FIG. 340

Basal-Cell Carcinoma.—This specimen was from a young female, age 18. There is marked hyperkeratosis. At the extreme margins are portions of normal epidermis but in the central area this has been largely replaced by a mass of deeply-staining cells of basal-cell type which also penetrate into the subjacent dermis. The downward projecting masses of basal-cells take the form of columns which are clearly defined from the surrounding stroma.

Hamilton and Ewen × 15



FIG. 341

Basal-Cell Carcinoma.—This shows in more detail the epithelial processes composed of relatively small, closely packed and deeply staining cells resembling the basal cells of the epidermis. Between them is an overgrowth of cellular fibrous tissue in which are blood vessels.

Hamilton and Ewen × 75



FIG. 342.

Basal-Cell Carcinoma.—This specimen shows a much larger tumour mass composed of many thick columns. They are well defined at their edges and within them are scattered small cystic spaces.

Hæmalum and Eosin. × 18.



FIG. 343.

Basal-Cell Carcinoma. The same as Fig. 342.—Part of a tumour mass showing the uniform character of the cells. At the invading edge the cells are more columnar in shape. In its substance are several small cystic spaces lined by columnar cells and containing coagulated albuminous fluid.

Hæmalum and Eosin. × 200.



FIG. 344

Basal-Cell Carcinoma (Cystic type).—The epidermis stretched and atrophied over the tumour which consists of two masses of basal cells. The centre of each mass is represented by large cystic space.

Haematoxylin and Eosin × 11

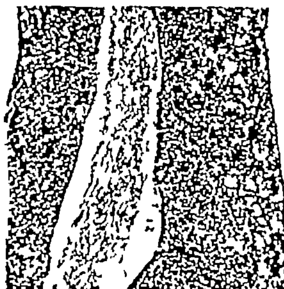


FIG. 345

Basal-Cell Carcinoma (Cystic type). *The same as Fig.* 344.—A portion taken from the adjacent parts of the two nodules. In the centre is strand of fibrous stroma. On either side are the masses of epithelium amongst which are little spaces due to degeneration of tumour cells. The edge of each cystic space shown in the low power (Fig. 344) appears at the margins of the illustration; it is formed by layer of flattened, atrophic tumour cells.

Haematoxylin and Eosin × 110



Fig. 347

Squamous Cell Carcinoma (Epithelioma).—From the lip. At the surface is small portion of unaffected epidermis which changes into the tumour formation by an abrupt dipping down into the dermis. Further over are many more irregular processes cut in various planes and in their central parts can be seen cornified areas, or cell-nests. In the dermis surrounding the tumour masses there heavy infiltration by chronic inflammatory cells of mononuclear type.
Haemalum and Eosin. ×40.



Fig. 348

Squamous Cell Carcinoma (Epithelioma). The same as Fig. 347—a cell-nest. In the centre whorl of epithelial cells undergoing keratinisation, around them are flattened squamous cells, and at the periphery are typical cells of rete mucosum type with intercellular bridges. A few inflammatory cells lie amongst the tumour cells, they are easily identified by their smaller size and darkly staining nuclei.
Haemalum and Eosin. ×400.



Fig. 349

Squamous-Cell Carcinoma (Epithelioma).—An early tumour with the downgrowths of epithelial processes still superficial and well-defined, but with typical central cornification ("cell-nests") in them.

Haematoxylin and Eosin × 45.

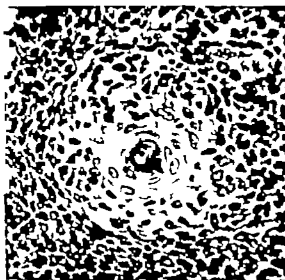


Fig. 350

Squamous-Cell Carcinoma (Epithelioma).—This tumour arose from a naevus sebaceus. A typical cell nest from one of the epithelial processes is shown.

Haematoxylin and Eosin × 400.

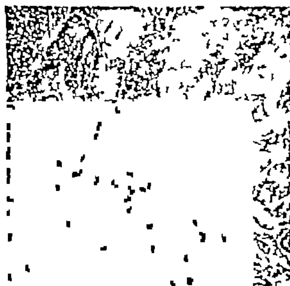


Fig. 351

Squamous Cell Carcinoma (Epithelioma).—In this example there is invasion of the dermis by abundant tumour tissue but central cornification is imperfect in them. There heavy infiltration of the stroma by chronic inflammatory cells.

Haemalum and Eosin × 70



Fig. 352

Squamous-Cell Carcinoma (Epithelioma). *The same as Fig.* 351. A portion of tumour process showing in substance small cell-nest surrounded by squamous epithelial cells. In the adjacent stroma are many chronic inflammatory cells—lymphocytes, plasma cells, and larger histiocytes.

Haemalum and Eosin × 400

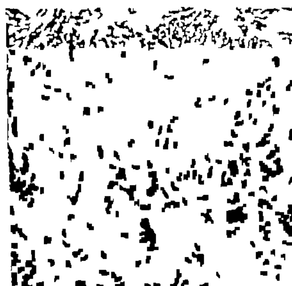


Fig. 353

Squamous-Cell Carcinoma (Epithelioma).—Anaplastic type. Only portion of an epithelial process is shown but it is typical of the others. There is no differentiation with formation of "cell-nests," the tumour cells being so closely packed that their squamous characteristics are difficult to determine. Many cells have mitotic figures in them which stain darker and are more compact than the ordinary nuclei.

Haemalum and Eosin. × 175.



FIG. 354

Squamous-Cell Carcinoma (Epithelioma).—This specimen was taken from the lip of a man, aged 64, who had a tumour there for three years. This is a portion of a more recent actively growing area. There is excessive surface cornification and thick ingrowths of tumour masses, most of which have extensive central degeneration with actual cornification in a few places.

Haematoxylin and Eosin × 20.



FIG. 355

Squamous-Cell Carcinoma (Epithelioma).—This shows in more detail the swelling and degeneration of the cells in the centre of the tumour process with an imperfect cell-nest at the side of one process.

Haematoxylin and Eosin × 80.



Fig. 356

Squamous-Cell Carcinoma (Epithelioma).—From the same patient as the specimen shown in Fig 354. This part of the tumour has been present for three years. It relatively benign epithelioma showing extensive degeneration in the central parts of the broad processes.

Hamilton and Eason 20

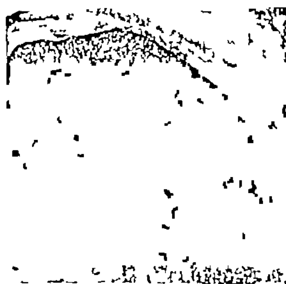


Fig. 357

Squamous-Cell Carcinoma (Epithelioma).—T shows in more detail portion of the tumour shown in Fig 356. I the centre is large area of debris formed by broken down tumour cells, outside of this is wide zone of poorly staining clear cells undergoing degeneration. At the periphery are the ordinary squamous cells fading into the zone of degeneration on the one side and sharply defined on the outer side by the fibrous stroma. A portion of the dermis included beyond this.

Hamilton and Eason 80.



Fig. 358.

Calcified Squamous-Cell Carcinoma (Epithelioma).—This was very slow growing tumour with extensive calcification. The epithelial processes are shown with masses of cornified debris in which are dark blue-staining deposits of calcium.

Haematoxylin and Eosin × 75.



FIG. 359

Squamous-Cell Carcinoma. Paraffin Carcinoma.—The epidermis hyperkeratotic. In the subjacent dermis there widespread infiltration by the epithelial processes of the tumour hich shew central cornification in the superficial area but little differentiation deeper—at the growing margin.

Hæmalum and Eosin × 12½



FIG. 360

Squamous-Cell Carcinoma. Paraffin Carcinoma.—*Deep part of the tumour shown in Fig. 359.* The epithelial processes are numerous, ill-defined, and composed of polygonal cells with no attempt at differentiation, an anaplastic type of squamous-cell carcinoma (epithelioma).

Hæmalum and Eosin 300



Fig. 351

X-ray Carcinoma.—There is much surface keratinisation and typical down-growths of epithelial processes, many of which have the usual central cornification. It is squamous-cell carcinoma (epithelioma).

Hamilton and Essex. × 20.



Fig. 352

Squamous Cell Carcinoma supervening upon Lupus Vulgaris.—No trace remains in the section of the original lupus, but the dermis is extensively infiltrated by an epithelioma which has undergone extensive cornification.

Hamilton and Essex. × 25.



Fig. 365

Cutaneous Horn.—A thick, hyperplastic layer of epidermis forms the base from which projects a pillar of hard keratinised material. This horn is fissured in the sectioning owing to its hard and tough character. Amongst the horny matter are blue-stained calcareous deposits. The unaffected epidermis of normal thickness is seen at the edges of the hyperplastic base.

Hæmalum and Eosin. ×7.



FIG 366

Intra-epidermal Carcinoma—*Paget Disease*.—The epidermal epithelium is invaded and largely replaced by the "Paget cells"—large, pale-staining clear cells. I[n] the surrounding dermis there is great inflammatory reaction in the form of granulation tissue heavily infiltrated with inflammatory cells

Hematoxylin and Eosin 65.

PSORIASIFORM CARCINOMA SHOWING DIFFERENT TYPES OF MALIGNANCY IN VARIOUS AREAS OF THE SAME LESION



Fig. 367

Psoriasiform carcinoma.—Here are seen downgrowths of the epidermis with the formation of processes and masses of epithelial cells, having the arrangement and characters of an epidermoid carcinoma of basal-cell type. *Hematoxylin and Eosin* × 100.



Fig. 368

Psoriasiform carcinoma.—In this area there is much hyperplasia of the epidermis, the cells of which are large and clear. The deeper layers are commencing to penetrate into the subjacent dermis and show an early attempt at central cornification. Here the malignancy is of the squamous epithelioma type. *Hematoxylin and Eosin* × 70.

PSORIASIFORM CARCINOMA SHOWING DIFFERENT TYPES OF MALIGNANCY IN VARIOUS AREAS OF THE SAME LESION



Fig. 369

Psoriasiform carcinoma.—This area shows only hyperplasia of the epidermis, with some parakeratosis superficially and excess of nuclei in its deeper layers. There is lymphocytic infiltration in the dermis. *Haematoxylin and Eosin.* ×110.



Fig. 370

Psoriasiform carcinoma.—There is marked parakeratosis. The rete pegs are hyperplastic, and a small area in the centre shows early malignancy with commencing [illegible]. *Haematoxylin and Eosin.* ×100.

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The black type indicates the principal reference

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